11

VOLUME 75 January 1956 NUMBER 1

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CONTENTS

Hydronephrosis *T. E. Gibson*
Pyelectasis. *Robert Lich, Jr., J. E. Maurer and M. L. Barnes*
Pelvic Fused Kidney. *A. L. Miller, Jr., A. W. Brown and G. C. Tomskey*
Osteogenic Sarcoma Involving Left Kidney *H. C. Hudson*
Ureteral Obstruction and Contractility in Man and Dog. *J. A. Benjamin, J. J. Bethell, V. M. Emmel, G. H. Ramsey and J. S. Watson* 25
Experimental Studies of Regeneration of Ureter without Intubation. *F. C. Hamm and S. R. Weinberg* 43
Use of Lock Splint in Intubated Ureterotomy. *J. R. Rinker* 52
A Basket Bougie for Extraction of Ureteral Calculi. *H. S. Browne* 55
Ectopic Ureter Opening into Seminal Vesicle *A. E. Goldstein and Eugene Heller* 57
Interstitial Cystitis: Treatment by Hydrocortone *T. L. Schulte and L. R. Reynolds* 63
Status of World War II Paraplegic. *K. H. Lord and R. C. Bunts* 66
Modified Position for Transurethral Resection of Bladder Tumors in Women. *R. A. Hancock* 73
Vesicovaginal Fistula. *B.-S. Azoury, P. L. Scardino and C. L. Prince* 75
Use of Vaginal Balloon Catheter for Stress Incontinence in Women. *C. A. W. Uhle and C. C. Mackinney* 79
Urethral Injuries. *S. D. Pelkovic* 81
Dilutional Hyponatremic Shock: Another Concept of Transurethral Prostatic Resection Reaction. *R. H. Harrison III, J. S. Boren and J. R. Robison* 95
Radical Retropubic Prostatectomy for Carcinoma. *Lylle Atherton and L. D. Atherton* 111
Prostatic Enzymes and Abnormal Bleeding *E. V. Z. Scott* 116
Primary Amyloidosis of Lower Genitourinary Tract. *J. H. McDonald and N. J. Heckel* 122
Cortisone in Treatment of Epididymitis. *T. J. Florence* 133
[illegible] ung Men. *Edward Gartman* 135
[illegible] "Prostatic" Serum Acid Phosphatase. *Gordon Mathes, [illegible] prunt* 143
Cystography in Children. *E. C. St. Martin, J. H. Campbell and C. M. Pesquier* 151
Abdominal Venography in Urological Diagnosis. *J. J. Kaufman, D. E. Burke and W. E. Goodwin* 160
New Technique of Translumbar Aortic Catheterization. *Jorge Cuellar* 169

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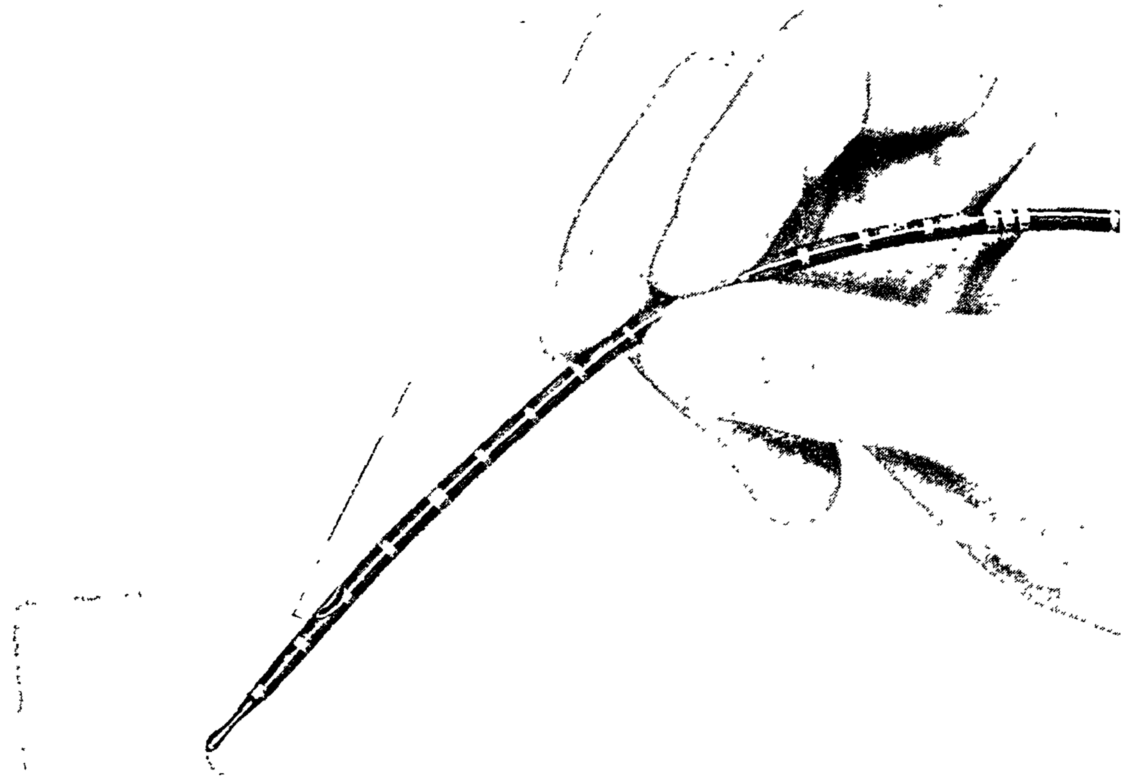

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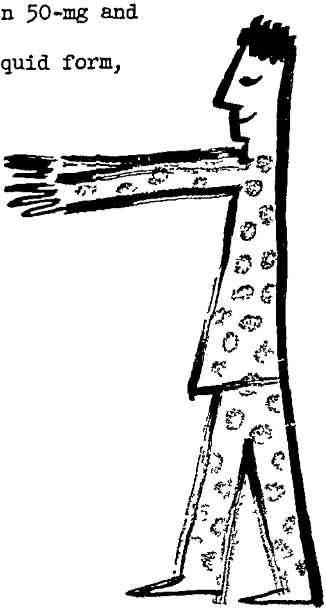

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The Journal of Urology is issued monthly. Two volumes are issued each year beginning in January and July.

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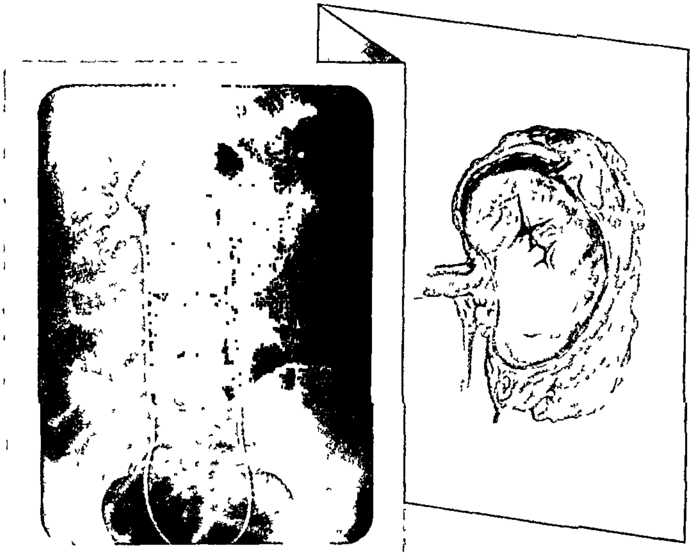

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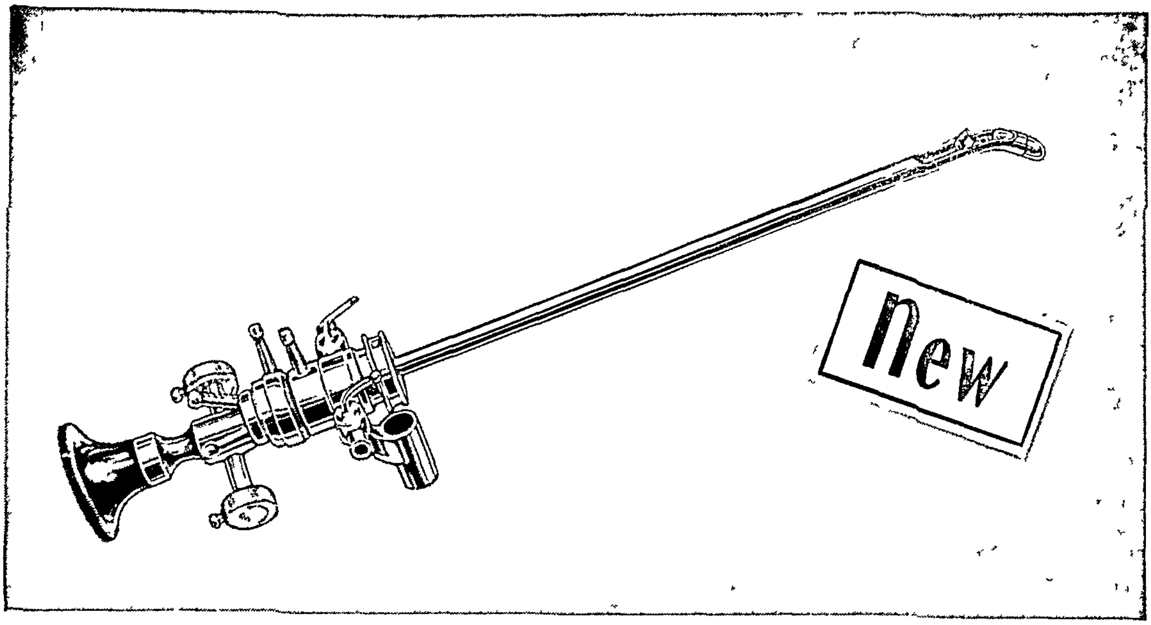

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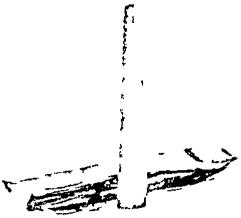

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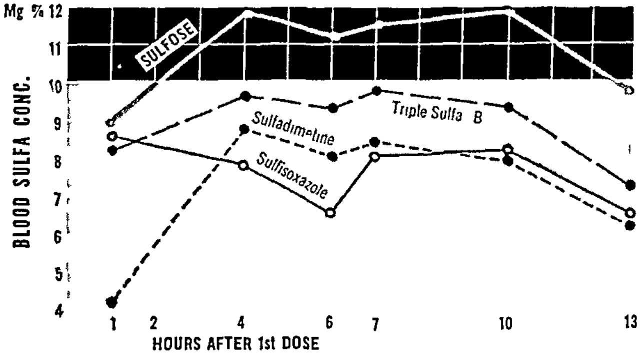

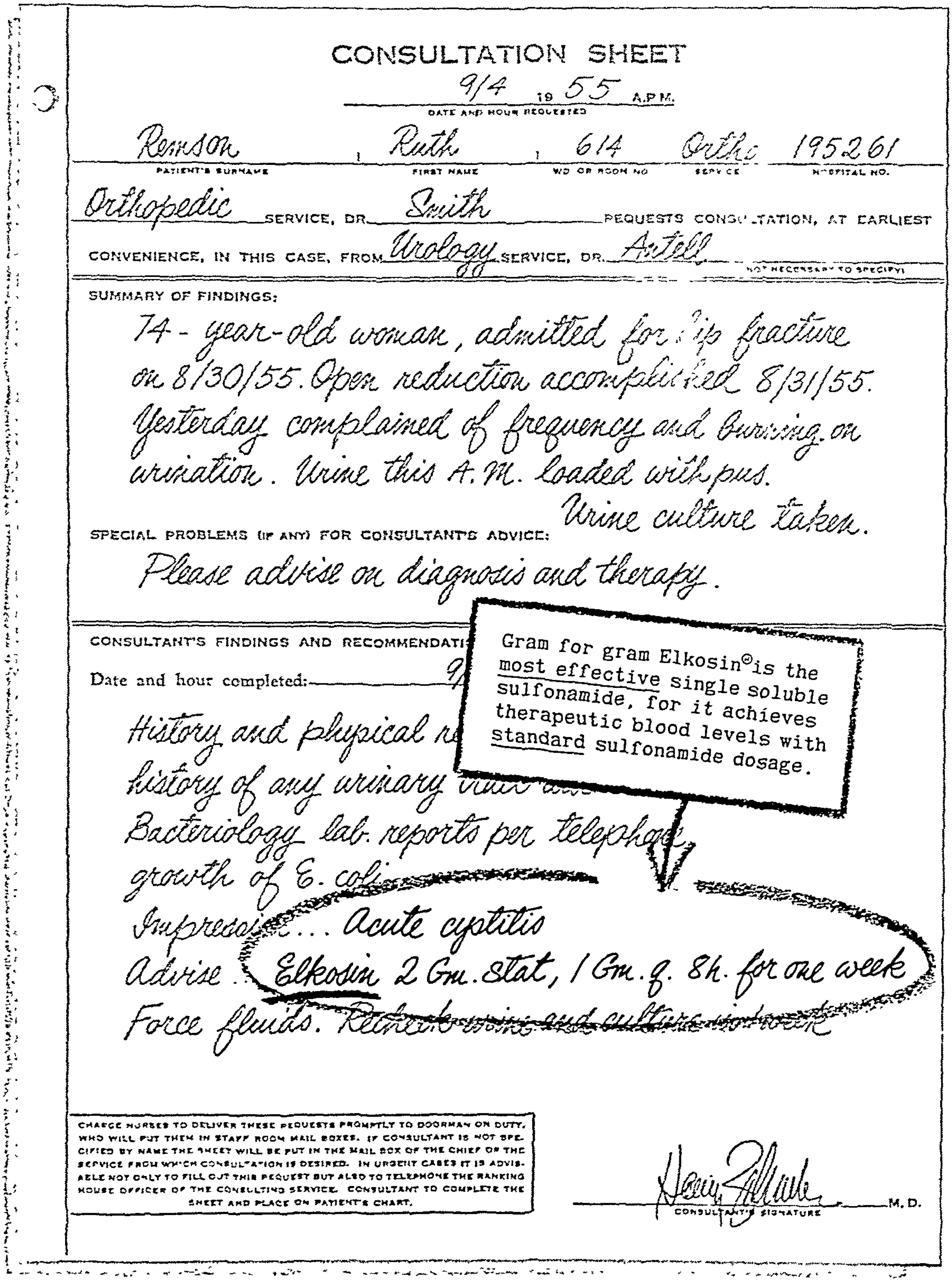

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9/4 19 55 A.P.M.
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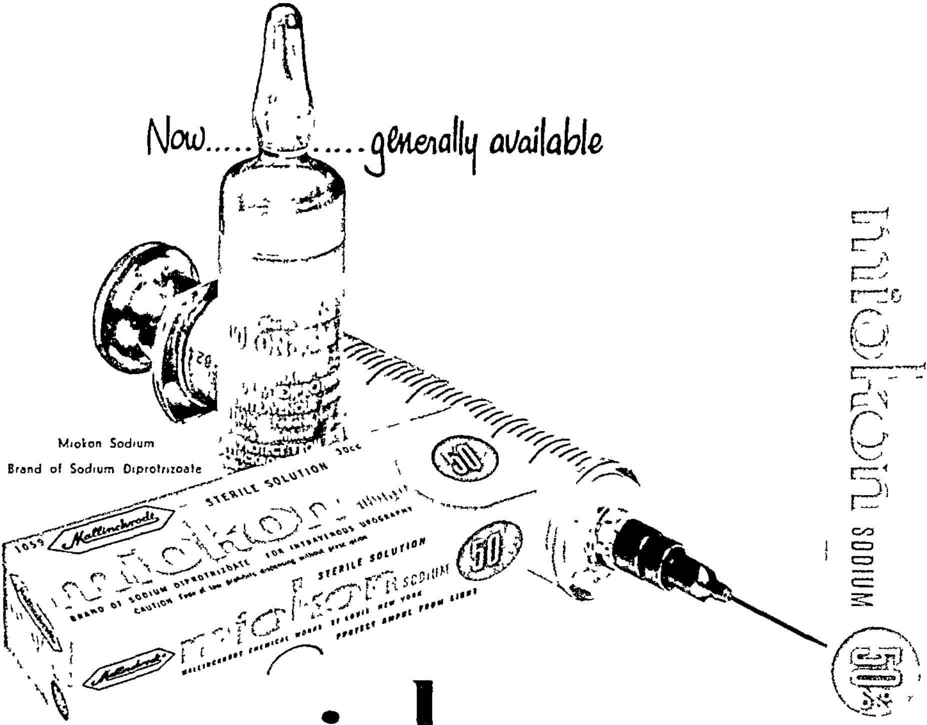

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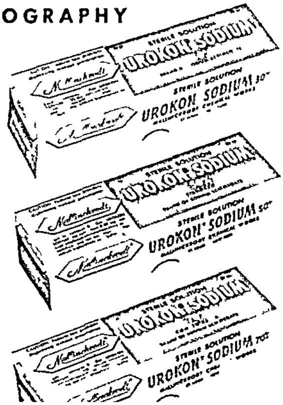

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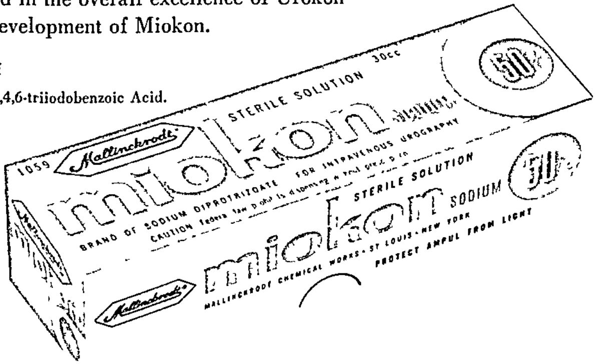

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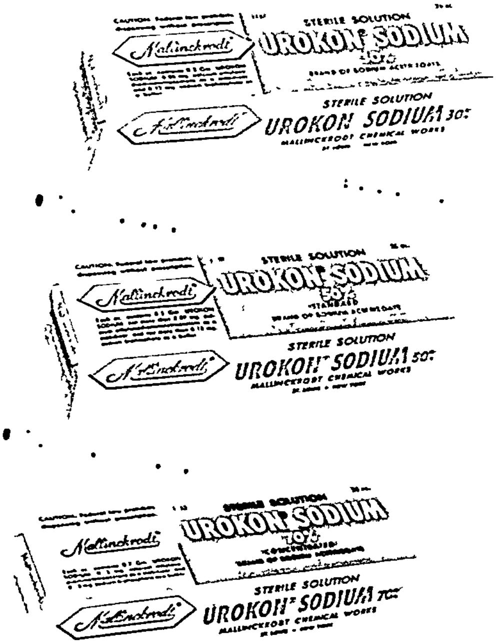

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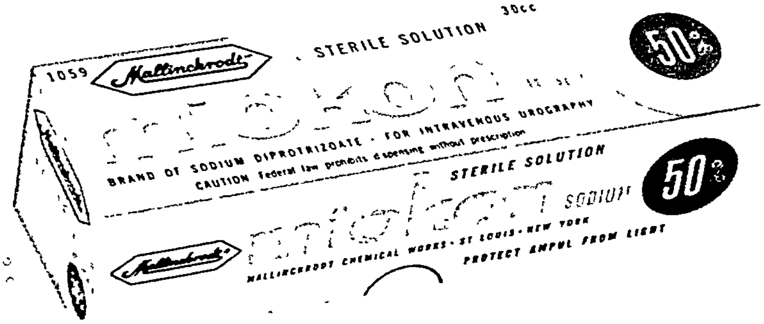
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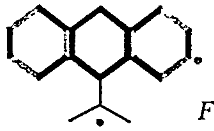

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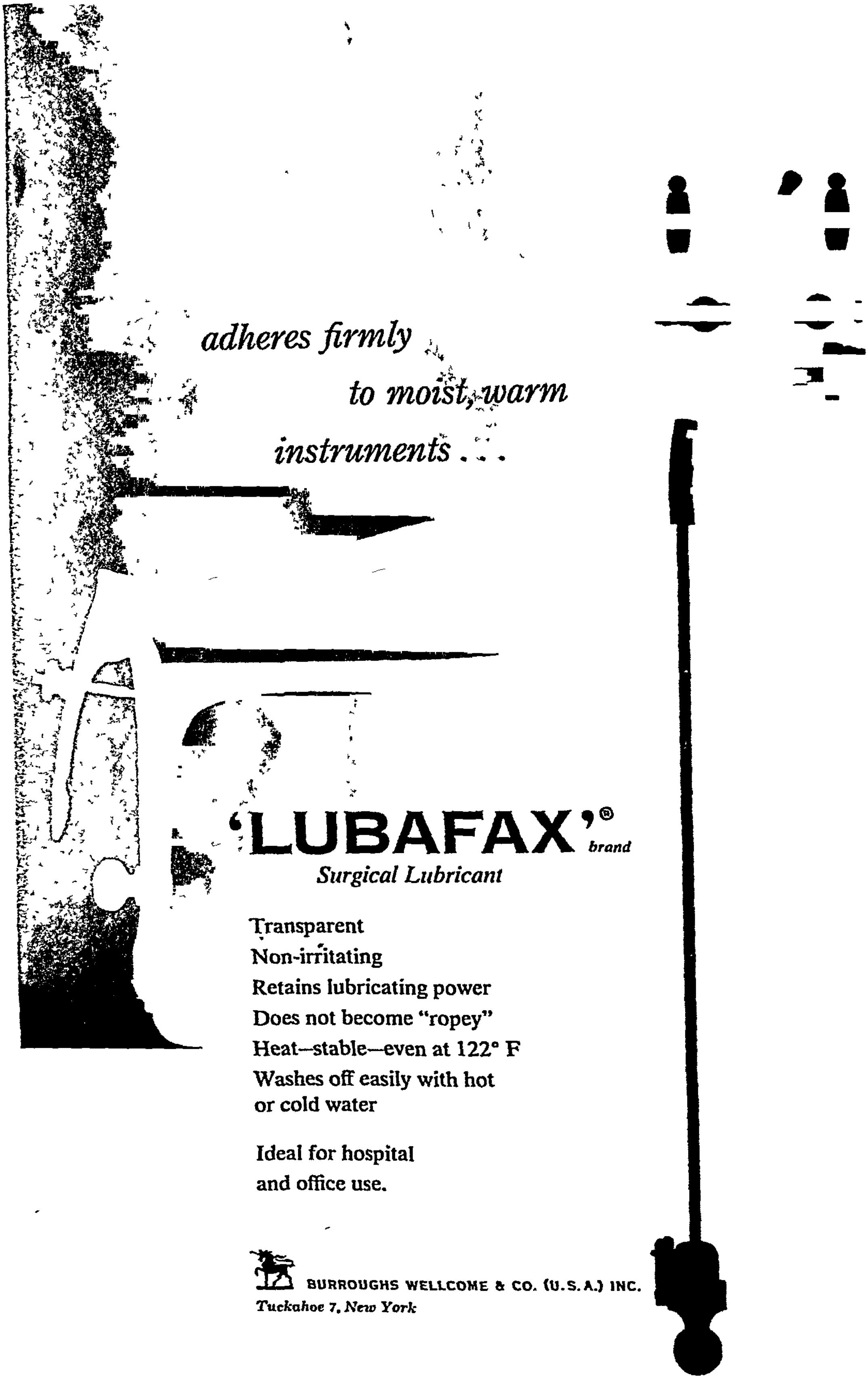

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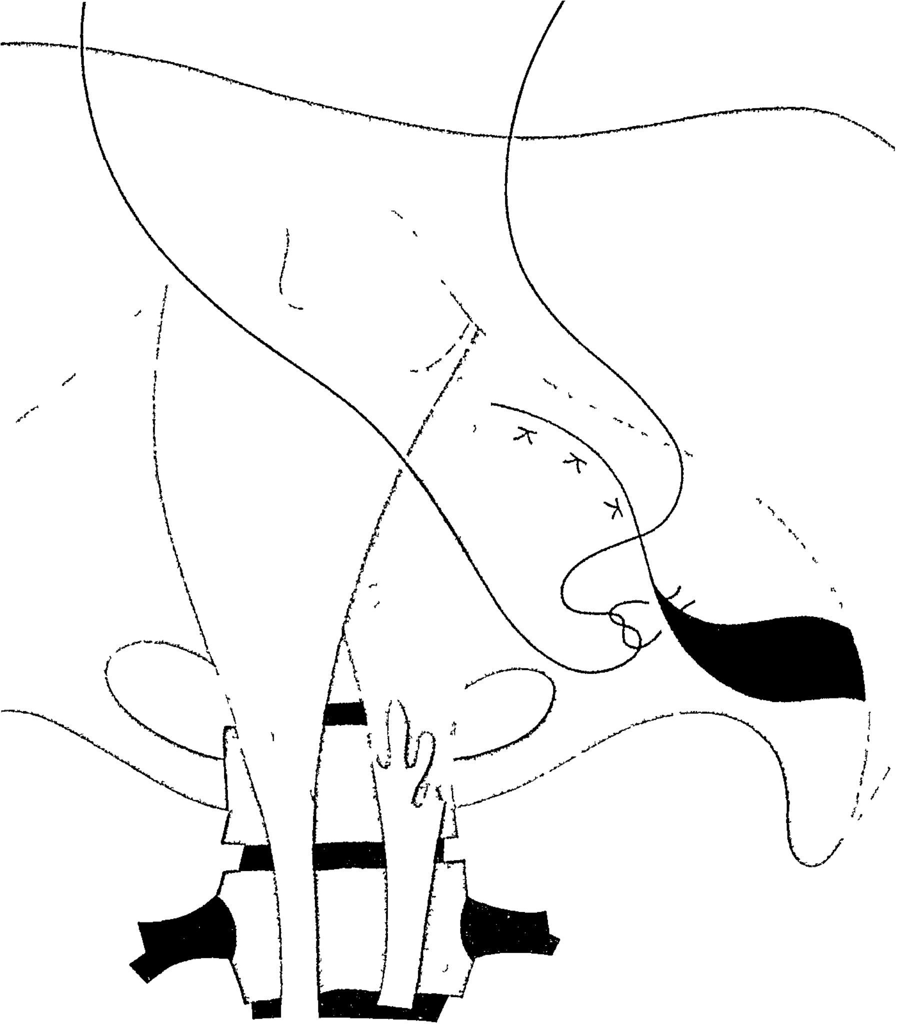

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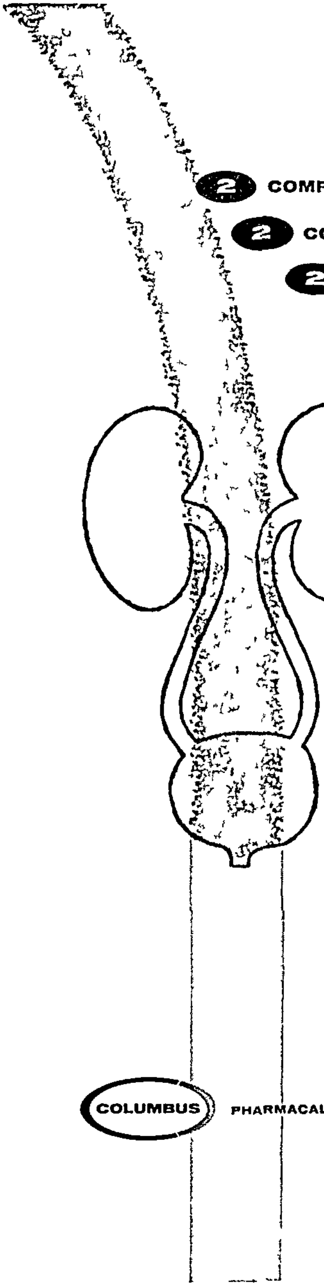

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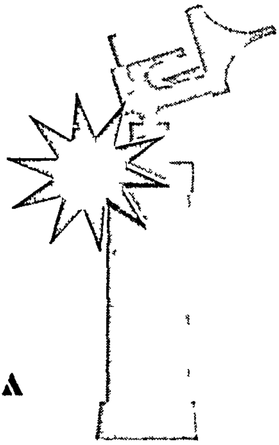

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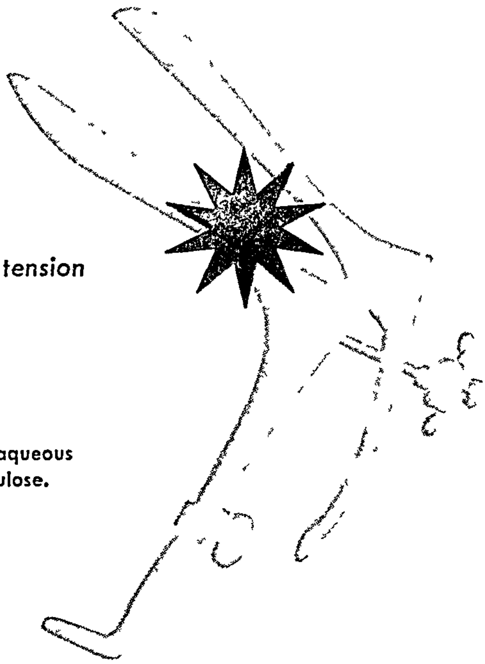

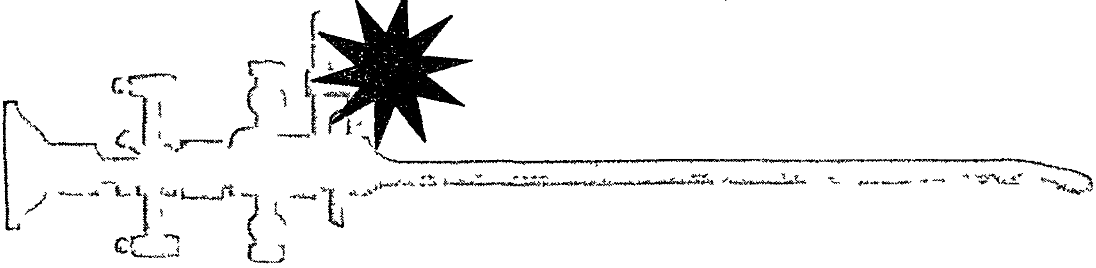

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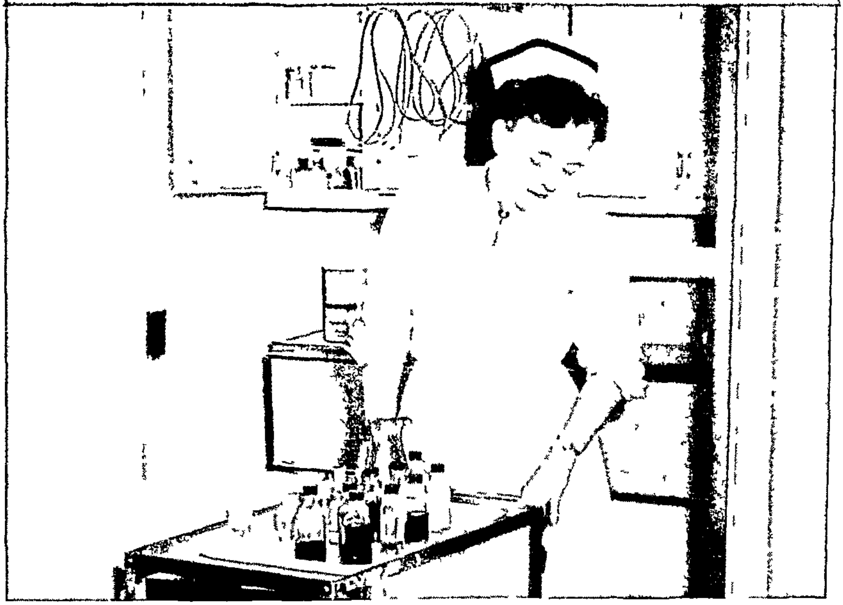

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*Breakey, R. S.; Holt, S. H., and Siegel, D.: J. Michigan M. Soc. *54*: 805, 1955.

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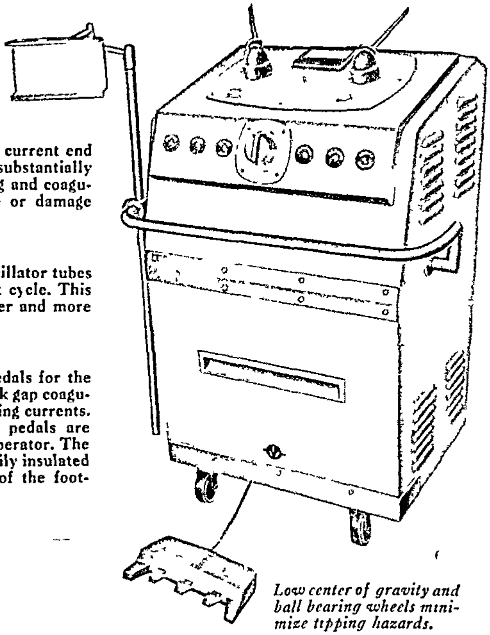

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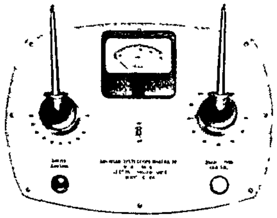

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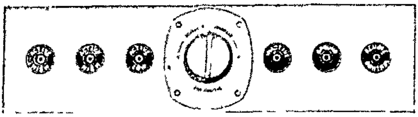

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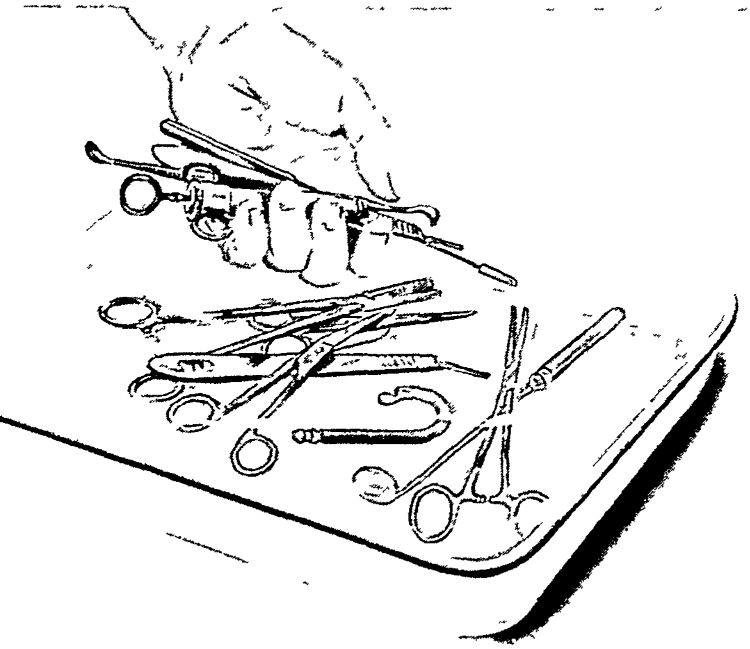

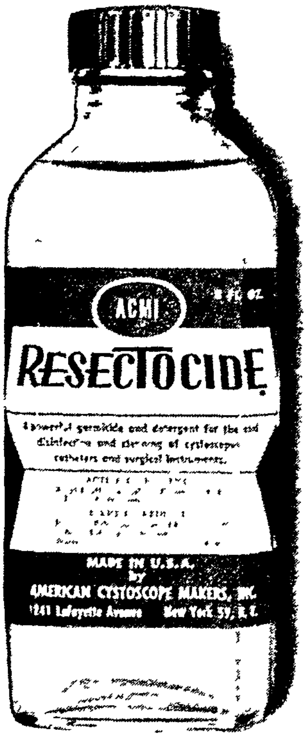
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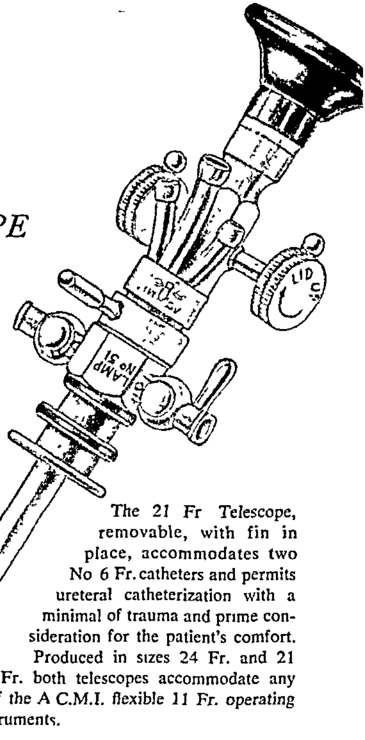

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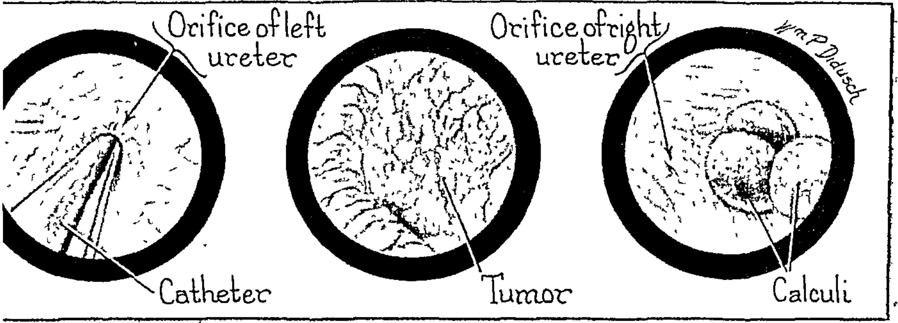

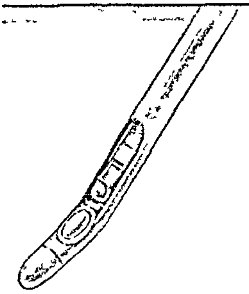

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The Journal of Urology
Vol 75 No 1, January 1956
Printed in U S A

HYDRONEPHROSIS DIAGNOSIS AND TREATMENT OF URETEROPELVIC OBSTRUCTIONS

THOMAS E GIBSON

Increasing interest in the management of ureteropelvic obstructions is clearly evident on perusal of the current medical literature It is gratifying to note that as a result of more widespread knowledge and experience with the many ingenious types of pyeloplasty, realization of the proper role of splinting and intubation, and the aid of potent drugs to combat infection, surgical conservation of hydronephrotic kidneys is being practiced with greater confidence and success and fewer kidneys are being subjected to nephrectomy Unfortunately the entire subject is still in an evolutionary phase and there are wide differences of opinion on various aspects of the problem

My purpose here is to discuss, and perhaps reconcile, divergent views on some of the controversial phases of diagnosis and treatment

DIAGNOSIS AND INDICATIONS FOR OPERATION

Diagnosis is not without its pitfalls, and demands the most meticulous attention to detail, because only a most complete urological study can answer the many questions arising in each individual patient as to whether or not the case requires surgery, and if so, whether some type of plastic procedure is indicated or *whether a nephrectomy should be done The successive steps of a complete* urological investigation should be carefully carried out, and many times a second confirmatory study done if there is the least doubt about the decision as to treatment The function of the hydronephrotic kidney is difficult to evaluate, as the following cases will illustrate

In figure 1 is shown the retrograde pyelogram of a man, 38 years old, whose right kidney exhibited a large hydronephrotic sac of 2000 cc capacity Preliminary excretion urography and retrograde study revealed that it had no function Following nephrectomy, I was nonplussed on finding that the kidney exhibited good parenchyma of almost normal thickness Furthermore, the urine from this kidney was sterile, an important factor which should always be evaluated An infected hydronephrosis in which there are chronic pyelonephritic changes, even though the hydronephrotic sac is small, is not likely to respond well to any type of pyeloplasty Thus, it is important to judge hydronephrosis not by its size but by the thickness of the parenchyma, and to note also whether the opposite kidney shows any degree of compensatory hypertrophy

The next case (fig 2), a man of 40 years, exhibited unilateral hydronephrosis of moderate size Excretory urography as well as retrograde study, in which separate renal function was determined by phenolsulfonphthalein excretion, revealed no function on the side of the hydronephrotic kidney The ureteral catheter was left indwelling for 24 hours and the phenolsulfonphthalein test repeated Quantitative output of dye, to my surprise, was practically normal It was then possible

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Read at annual meeting Southeastern Section of American Urological Association New Orleans La March 20 24 1955

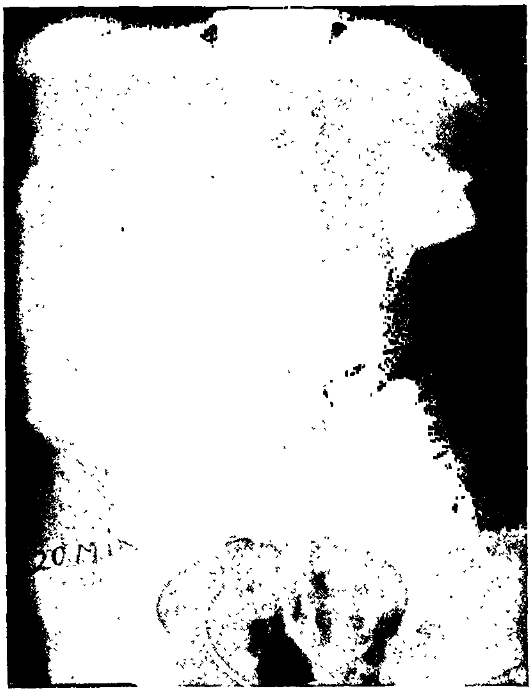

FIG. 1. Right hydronephrosis, 2000 cc capacity. Intrinsic ureteropelvic obstruction of unusual type, consisting of miniature bicuspid valve simulating mitral valve of heart.

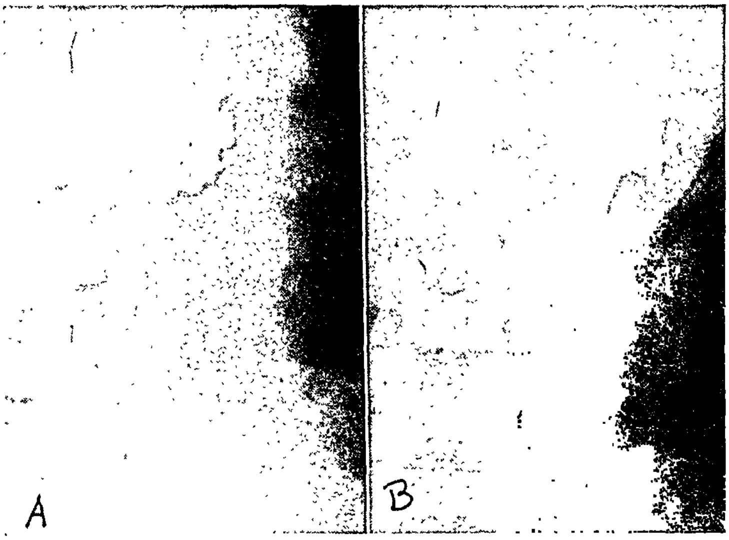

FIG. 2. *A*, hydronephrosis (left). Initial study showed only trace of PSP excretion. After 24 hours catheter drainage, PSP excretion almost normal. *B*, pyelogram made 6 months after operation. Ureteropelvic obstruction was entirely extrinsic, so no splinting or intubation was used.

to do a successful pyeloplasty without resorting to nephrectomy. When excretory urography fails to outline the kidney pelvis it is good practice to repeat the roentgenogram in 4 hours, or even 24 hours if there is no evidence of excretion in the first hour.

It has been said that a hydronephrotic kidney which cannot by physiological tests perform 25 per cent of total renal function is not worth conserving, although there are exceptions to all rules. This statement is based on the assumption that a kidney to be worthy of conservation should be able to carry the total load should it ever become necessary. Such a rule cannot be followed too rigidly for two reasons. First of all, the difficulty of accurately determining the function of the damaged kidney prior to surgery is obvious, and to estimate the potential function of the kidney after surgery is still more difficult. In the second place, one can readily conceive of a situation in which some intercurrent pathological change might compromise the function of the contralateral organ so that the increment of function in the repaired hydronephrotic kidney, however small, say even 5 or 10 per cent, might contribute sufficiently to the total function to sustain life. The ultimate decision in questionable cases in my experience is frequently reserved until the time of surgery. If the parenchyma is reasonably healthy in appearance and has a thickness of one centimeter or more, it is conserved rather than removed. If one is dealing with a solitary kidney or a case in which the opposite kidney is hydronephrotic or pathological from any cause, then conservation is of course mandatory even though it may have only a trace of function. The solitary kidney requiring pyeloplasty responds surprisingly well compared to a similar kidney having a healthy mate, a fact which tends to support the doctrine of renal counterbalance. Obviously, excretory urography does not give us all the information we should have, and may be actually misleading. The corroborative findings of retrograde pyelography are most essential and it is helpful to do both a ureteropyelogram and a pyeloureterogram. The former is done by inserting either a Braasch bulb or Garceau catheter into the lower ureter and injecting radiopaque media. This will usually outline clearly the obstructed area and give some idea of its character. Then an ordinary ureteral catheter is passed to the kidney pelvis, provided it will pass the obstructed area, and a pyelogram is done. On withdrawal of the catheter, a delayed film is exposed. Ordinarily a normal, unobstructed kidney pelvis should show no retained medium after ten or fifteen minutes. The danger of lighting up an infection in the affected kidney is negligible at the present time, using aseptic technique and prophylactic medication with urinary antiseptics.

Another diagnostic pitfall deserves emphasis at this point. As a result of the widespread use of excretory urography, many unsuspected instances of hydronephrosis of varying degree are being discovered. It may be difficult in some cases to distinguish between the large normal pelvis and an early hydronephrosis. The distinguishing point, as mentioned by O'Conor, is the fact that a true hydronephrosis will show blunted minor calyces whereas in the kidney with an abnormally large pelvis the minor calyces will exhibit their normal sharp cupping.

Another phase of the diagnosis and evaluation of hydronephrosis which has been neglected, or at least not sufficiently emphasized, is the problem of progression versus nonprogression of the disease. We are accustomed to think in terms of experimental hydronephrosis in which ureteral ligation leads invariably to progressive hydronephrotic changes in the kidney. Growing experience has proved that this is not invariably true in clinical practice. In some instances where

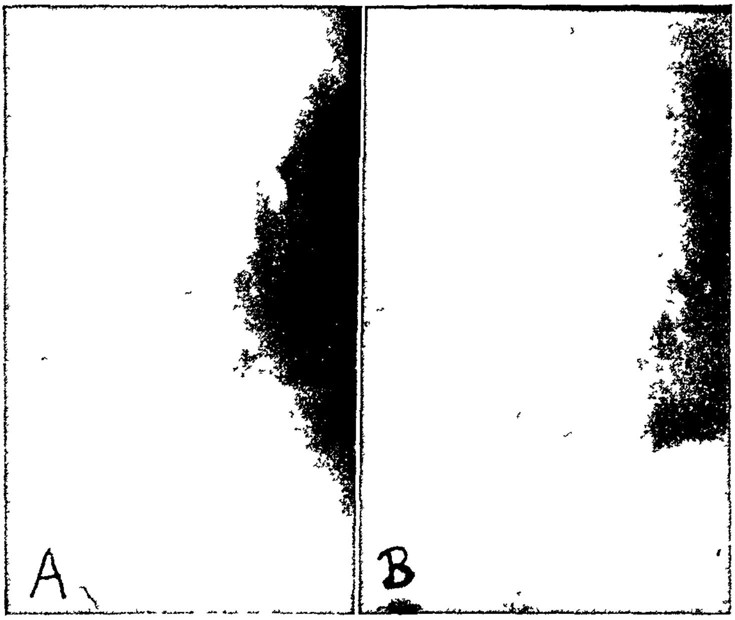

FIG. 3 *A*, pyelogram (left). An example of static or nonprogressive hydronephrosis. *B*, pyelogram made in same case 12 years later. This patient was not operated upon, and had no treatment other than passage of diagnostic catheter for purpose of pyelography Dilatation appears to have regressed rather than progressed.

operation had been deferred, it has been found that over a period of years there has been no advance in the degree of hydronephrosis, the condition becoming static or nonprogressive. Mention of this fact has been made by Hellström, Giertz, and Lindblom (1949) and O'Conor (1954). Hoyt (1954) speaks of the condition as "Equilibrium in Hydronephrosis." Pyelograms in cases of this kind are shown in figures 3, 4, 5, 6 and 7. This concept presents clinical implications which require reappraisal of our views concerning prognosis and therapy. Unquestionably, many cases of hydronephrosis are congenital in origin, yet are not diagnosed until adulthood is attained. Over this long period of years the hydronephrotic sac would reach enormous proportions were it not for the fact that there are counteracting forces at work tending to relieve it. Giant hydronephroses are rare, and one wonders what mechanism comes into play to produce a massive hydronephrosis containing 18 liters, as was recently reported by Earlam (1950).

Recognition of the fact that hydronephrosis in some instances may reach equilibrium and become nonprogressive should restrain the too eager surgeon from unnecessary intervention. Conservative treatment should consist in watchful waiting for a period of months, or even years, if the condition remains asymptomatic and excretion urographic outlines remain unchanged. If appreciable functional impairment, pain, urinary infection, or reflex gastrointestinal symptoms develop, then surgery should be done without further delay.

TREATMENT

Pelviureteroplasty. When surgical intervention is deemed necessary, after careful diagnostic appraisal, the surgeon is faced first of all with the decision as

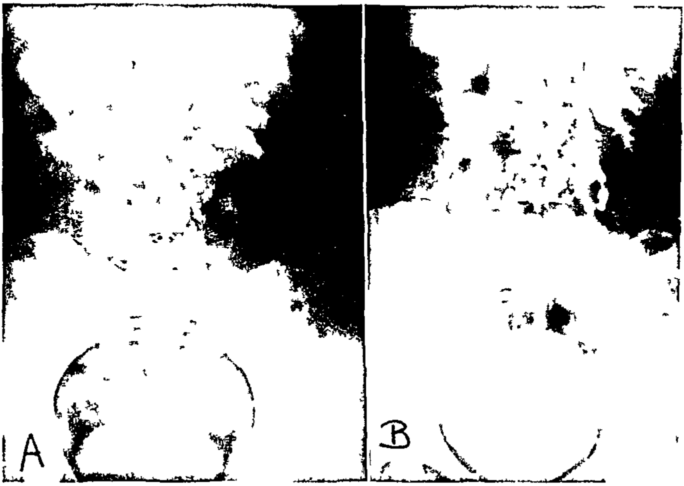

FIG 4 Another example of equilibrium or nonprogression in hydronephrosis This is a 34 year old woman There is an interval of 9 years between the two pyelograms (*A* and *B*) Patient had no surgery or other treatment (Courtesy of Dr J L Goebel)

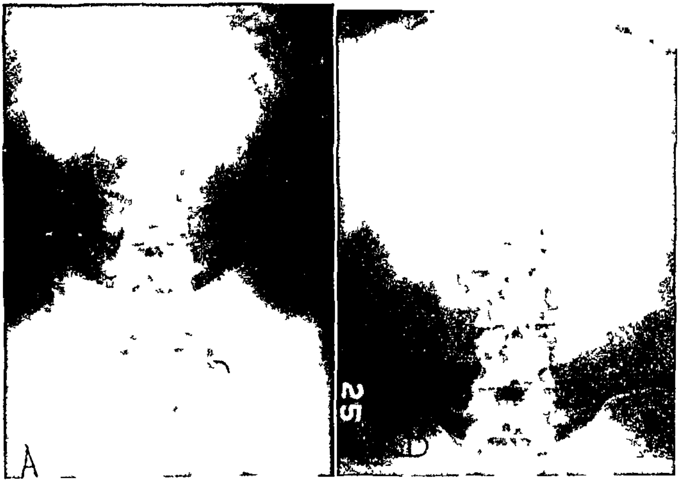

FIG 5 Another example of nonprogression in hydronephrosis There is an interval of 8 years between pyelograms *A* and *B* Patient likewise had no treatment, surgical or otherwise *(Courtesy of Dr Spencer Hoyt)*

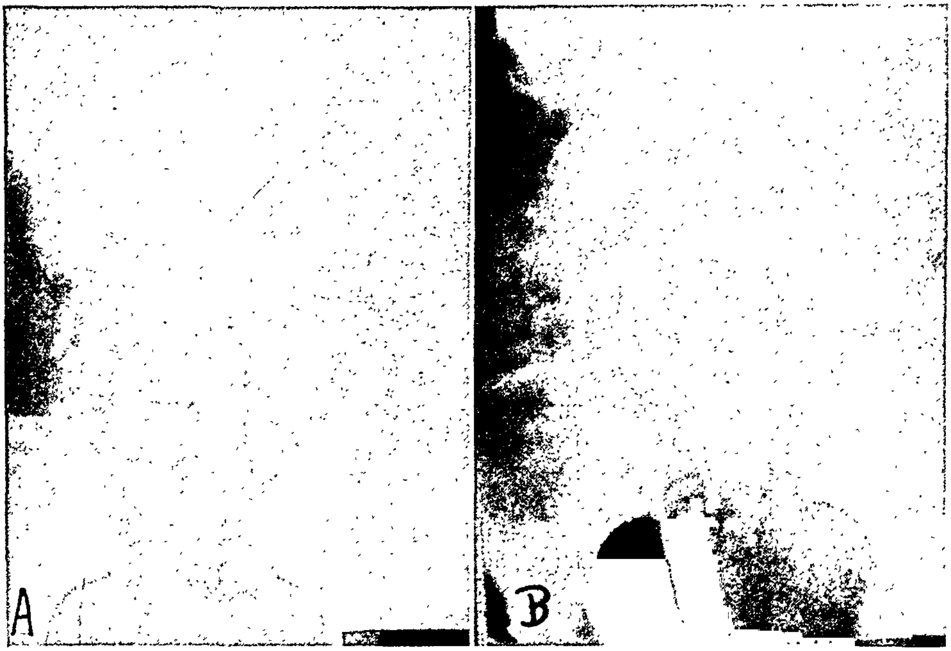

FIG. 6. Another example of nonprogressive hydronephrosis (right). There is an interval of 9 years between pyelograms *A* and *B*. Sharp cupping of calyces would seem to indicate that this is probably an instance of a kidney with a large pelvis rather than a true hydronephrosis. (Courtesy of Dr. Spencer Hoyt.)

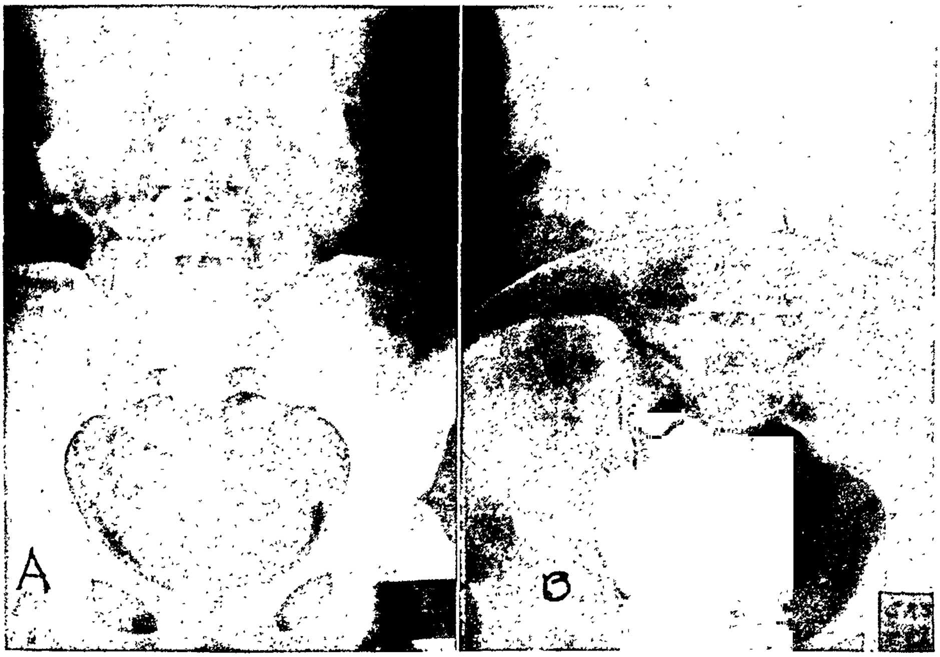

FIG. 7. Another example of hydronephrotic equilibrium. There is an interval of 13 years between pyelograms *A* and *B*. (Courtesy of Dr. Spencer Hoyt.)

to whether to perform a nephrectomy or attempt some corrective plastic procedure. Solution of the problem of treatment is easy when one kidney is normal and the opposite kidney has reached the end stage of hydronephrotic atrophy. A nephrectomy is then advisable and can be done with little risk or mortality. However, many are borderline cases which will call forth all the experience and skill that the urologist can muster to come to a proper decision as to treatment. He should be thoroughly familiar with the many ingenious surgical procedures used in plastic repair of ureteropelvic obstructions. He must likewise be thoroughly familiar with the various methods of splinting and intubation in common usage, with their indications and contraindications. (These have already been reviewed in my preliminary lantern slide demonstration.)

Time does not permit evaluation of all these procedures. The choice of operation depends upon the nature of the obstruction. It so happens that several types of pyeloplasty may be applicable to one type of obstruction and one's choice depends upon individual preference. A parallel situation exists with bladder neck obstructions which can be treated by several procedures depending upon the surgeon's individual preference. The principal types of pyeloplasty and ureteral splinting were published by the author in 1945. In 1952, in conjunction with Schwartz and Hewitt, an evaluation of results was published. Different methods were used successfully, but in general, for the majority of cases, we found a modified Davis procedure the most satisfactory. This consisted of nephrostomy drainage with a Foley catheter, simple longitudinal incision through the obstructed area and intubation with polyethylene tubing throughout the entire course of the ureter. No sutures were used. The results were uniformly good, and we felt that, because of its simplicity and speed of performance, it was generally preferable to flap operations requiring meticulous and tedious suturing.

The so-called Y plastic, or Foley modification of the Schwyzer pelvioureteroplasty has many enthusiastic adherents, both here and abroad. It is particularly useful in cases of high insertion of the ureter in the pelvis with valve-like formation. The more recent operation of Culp and DeWeerd (1951) appears to be a further elaboration of the Y plasty, and the operation of Scardino and Prince (1953) is practically identical with that of Culp.

In cases of large extrarenal pelves, radical excision of the entire pelvis including the ureteropelvic junction and reanastomosis of the ureter to the lower end of the pelvis has been advocated by Priestley, McIver, Deming and others. Dorsey (1954) recently reported an interesting modification of this procedure in which the pelvis is completely resected and reanastomosed above the level of the ureteropelvic junction. The latter is then longitudinally incised and intubated according to the method of Davis. This obviates the danger of stricture formation at the site of reimplantation of the ureter into the pelvis, as might happen in the Kuester operation (1892) and other types of ureteropyeloneostomy.

Ureteral splinting and intubation. The ultimate goal of all plastic procedures for the correction of ureteropelvic obstruction is to permanently relieve the patient of all discomfort, to promote permanent emptying of the kidney pelvis without stasis, and optimum renal function without the presence of residual infection.

The perfect operation would be one requiring neither drainage nor splinting. Unfortunately, this ideal appears to be unattainable in the majority of cases. Opinion is divided on this point between the "splinters" and the "nonsplinters". In previous publications (1939, 1940, 1945, 1952 and 1954) I have emphasized the importance of splinting as a necessary corollary to pelvioureteroplasty in order to insure a successful outcome for the vast majority of cases. Reference to the literature shows that most urologists concur in this opinion. However, there are dissenters, notably Bischoff (1953) and Hamm and Weinberg (1954) who state that these cases can be operated upon successfully without the use of splinting and nephrostomy tubes. Hamm and Weinberg state that adequate drainage is obtained by leaving a vent in the renal pelvis. Furthermore, they maintain that the strictured area can be treated by simple linear incision without splinting or intubation, and that healing by primary intention with adequate caliber will result.

Perhaps the pendulum has swung too far in favoring the doctrine of universal splinting, but I feel that over a period of years it has been the most important factor in the successful outcome of a great many cases, and I would be very reluctant to abandon it except in certain cases of extrinsic obstruction. Splinting or intubation (synonomous terms) have often been the determining factors which have given me the necessary courage to attempt a plastic procedure in difficult cases that I might otherwise have subjected to nephrectomy. I feel that intubation is essential in those cases presenting an elongated type of stricture at the ureteropelvic junction such as Davis (1951) has described.

Certainly no one can deny that it is absolutely necessary in those occasional cases in which there is a complete avulsion or dissolution of continuity of the ureter. The report of Howard and Hinman (1952) is illuminating in this respect. Two cases have occurred in personal experience, one in a case of solitary kidney in which the ureter had been destroyed for a distance of two or three centimeters below the ureteropelvic junction. In both instances the gap was bridged solely by intubation which acted as a scaffolding for the regeneration of the ureteral wall. The intubation was maintained in these cases for seven weeks. Less flagrant cases may require splinting for periods of one to three weeks depending upon their severity. An excellent result was obtained in both cases as shown by urograms made 1 and 2 years later. Experiences such as these attest to the wonderful capacity of the ureter to regenerate. That this regeneration is not simply a tube of fibrous tissue has been proved by several independent investigators who have demonstrated the ability of the ureter to regenerate and fill in large gaps not only with connective tissue but also with smooth muscle and mucosa as well. Your attention is directed particularly to the experimental work of Davis, Strong and Drake (1948), Weaver and Henderson (1953), Lapides and Caffery (1955), and Boyarsky and Duque (1955).

One of the main objections to splinting and intubation is the tendency for infection to occur when a foreign body is left in the urinary tract for any period of time. I have not found this a serious consideration, because in personal experience infections have been of minor degree and have cleared up promptly with proper therapy soon after removal of the splinting and drainage tubes During the splinting period I have not often resorted to irrigations but O'Conor advises frequent instillations of 15 to 30 cc of 0 1 per cent aerosporin solution to combat Pseudomonas aeruginosa, and also daily subcutaneous injections of 300 units of hyaluronidase to keep the urine clear and prevent encrustation The use of polyethylene tubing, as shown by Schlumberger and Riparetti (1952) has proved to be of value in reducing the latter possibility to a negligible factor

A fair percentage of cases of ureteropelvic obstruction will be found to be purely extrinsic in nature, due to congenital fascial bands and adhesions and occasionally to an anomalous artery or vein Correction of extrinsic factors may be sufficiently curative without having to resort to splinting Blood vessels may obstruct *primarily but in most cases some other factor will be found to be the* primary cause of the obstruction Even though the obstruction may appear to be entirely extrinsic, it is always wise to calibrate the ureteropelvic outlet so as not to overlook a possible intrinsic obstruction, such as a stricture of the ureteropelvic junction, which might be of even greater importance than the extrinsic in a given case This is easily accomplished by either opening the pelvis and calibrating it with a Mayo hemostat, Braasch bulbs, or by injecting water into the pelvis through a needle attached to a large Luer syringe One can observe in this way how readily the pelvis empties itself

Even in intrinsic obstructions, such as a stricture of the ureteropelvic junction of minor degree, it is not always necessary to splint Such a case is illustrated in figure 8 A 6-year-old girl suffered repeated attacks of acute pyelitis and had a stricture of the left ureteropelvic junction This was corrected by a double Fenger type operation This is done as described by the author (1945) by transfixing the ureteropelvic junction longitudinally with a No 11 scalpel blade which passes through both sides of the obstructed area simultaneously The double incision is made long enough to extend beyond the area of narrowing The incision is closed transversely with 5-0 chromic gut on an atraumatic needle, according to the Heineke-Mickulicz principle This operation is preferable to the original Fenger operation which often failed due to postoperative buckling at the site of incision Splinting is not necessary in this so called double Fenger or trans fixion operation

Another factor which should not be overlooked in plastic procedures is nephropexy The hydronephrotic kidney often undergoes more or less ptosis and torsion which are conducive to ureteral kinking Suspension of the kidney will cause the ureter to heal in good alignment and afford the kidney pelvis more adequate dependent drainage The Deming type of nephropexy is admirably suited to those cases requiring suspension

For the purpose of splinting or intubation, it is now possible to obtain polyethylene tubing in various calibers of the right degree of flexibility It is in general preferable to rubber or latex because of its nonirritating and nonencrusting qualities In former years my experiences with the Cumming and

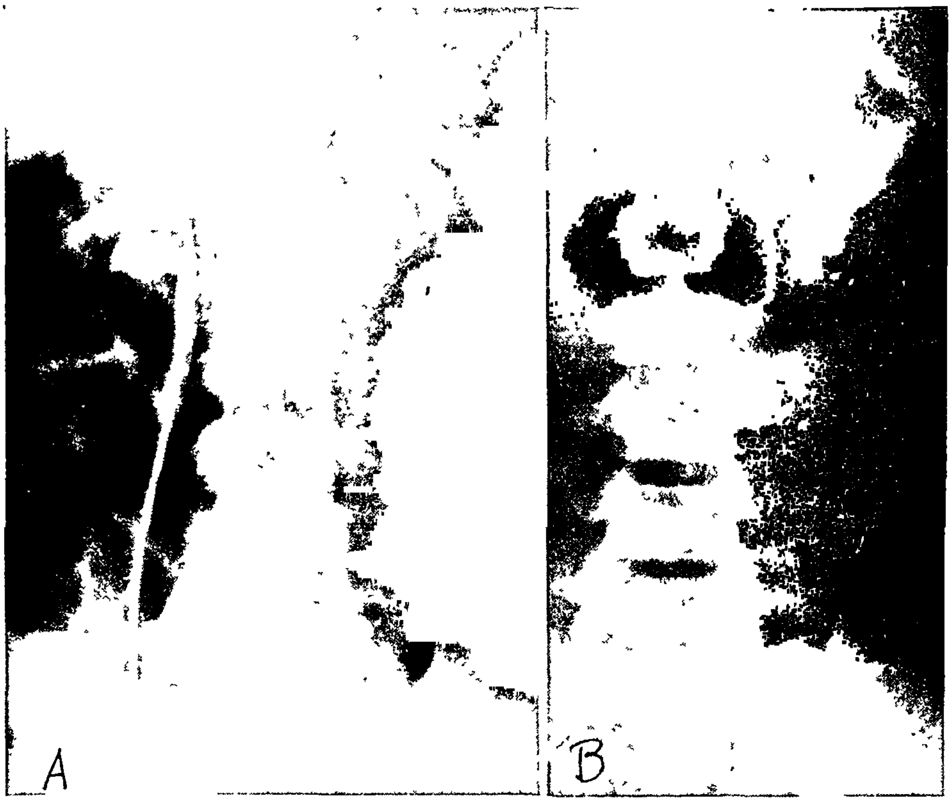

Fig. 8. A, hydronephrosis (left) in 8-year-old girl due to a combination of extrinsic fascial bands and intrinsic stricture. *B*, pyelogram (left) showing result of pyeloplasty 6 months postoperatively. Stricture was treated by a double Fenger (transfixion) type of operation. This is type of case in which splinting or intubation was not deemed necessary

the McIver combination nephrostomy and splinting tubes were not satisfactory because they were made of soft flexible latex, and tended too easily to crawl out of the ureter and become displaced. However, a polyethylene Cumming tube is now available which promises to obviate this difficulty, since it has more rigidity. The T tube type of splinting favored by Deming has its merits in certain cases.

Thus, one has a rather wide choice of splinting, as well as plastic procedures with which the operator should be familiar in order that he may utilize the procedure that will be best for the individual patient.

SUMMARY

The management of ureteropelvic obstructions is discussed with special emphasis on diagnosis and indications for operation.

Particular stress is placed on the differentiation of the normal large pelvis and the small hydronephrotic pelvis, as well as the problem of "progressive" versus "nonprogressive" hydronephrosis. Emphasis on these phases of the problem injects clinical implications requiring reappraisal of our views concerning prognosis and therapy. It has been shown that many patients with varying degrees of hydronephrosis may not require operation, and may be kept under observation for an indefinite period of time provided the hydronephrosis remains nonprogressive and devoid of symptoms or infection

When surgery becomes necessary the surgeon should be guided as to his choice of procedure by the most thorough and, if necessary, repeated preliminary urologic studies Careful functional evaluation of both kidneys is of paramount importance

The operator should be thoroughly familiar with the various methods of plastic repair and splinting so as to be capable of applying the procedure best suited to the individual problem at hand

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THE JOURNAL OF UROLOGY
Vol. 75, No. 1, January 1956
Printed in U.S.A.

PYELECTASIS

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Pyelectasis or dilatation of the renal pelvis and calyces is occasioned by the interference of urine drainage through the upper ureter. Ureteral dysfunction in the upper ureter may be of three types: 1) ureteral obstruction confined to the ureteropelvic junction, 2) an extended ureteral stricture or 3) inadequate segmental ureteral peristalsis. Our remarks will be confined to obstructions at the ureteropelvic junction; the type that is usually referred to as being due to a fibrous band or an aberrant renal vessel. It is our purpose to present for your consideration a method for the repair of ureteropelvic obstructions and secondarily to briefly mention some of our work on the basic etiology of these obstructions.

The stimulus that initiated the study of etiology occurred in 1937 when it was noted that whenever a fibrous band or aberrant vessel was divided that was presumably obstructing the ureteropelvic junction, a curative result did not invariably follow and a secondary nephrectomy occurred all too often. It was obvious that in many instances the vessel or band was not the primary cause of the pathological process.

It was observed that antegrade or retrograde calibration of the ureteropelvic junction, at the time of surgery, did not necessarily reveal an obstruction and even in the event of an adequate ureteropelvic caliber the pyelectasis on occasion progressed postoperatively. Furthermore, that fluid could be readily injected into the renal pelvis retrograde was generally recognized; however, if at operation the renal pelvis was filled with fluid, by injection into the pelvis through a needle, the fluid would not readily escape down the ureter.

To undertake a study of this problem it was necessary to resect the ureteropelvic junction to obtain the specimen for histological study. After many fruitless observations and unavoidable interruptions one of us (M. L. B.) noted, in some instances, valve-like structures within the ureteropelvic lumen when the specimens were cut longitudinally.

The number of such specimens examined to date is 15 and of this group nine showed distinct valve formation. In the remaining 6 specimens there were four that showed suggestive valve formation and two in which there was marked thickening of the ureteral wall with increased fibrous and muscle tissue and leukocytic infiltration. In the group of nine showing valve formation, it was noted that there was at the ureteropelvic junction an angulating vessel or fibrous band present at the time of surgery in 5 instances. In the group of 6 not having definite valves present, there were 2 instances of vessel or fibrous band obstruction.

We have no instance in this series in which the vessel or band acted as the primary cause for pyelectasis; however, there is little doubt that this can and does exist on occasion.

In the surgical treatment of pyelectasis one must deal with a dual process:

Read at annual meeting, Southeastern Section of American Urological Association, New Orleans, La. March 20-24, 1955.

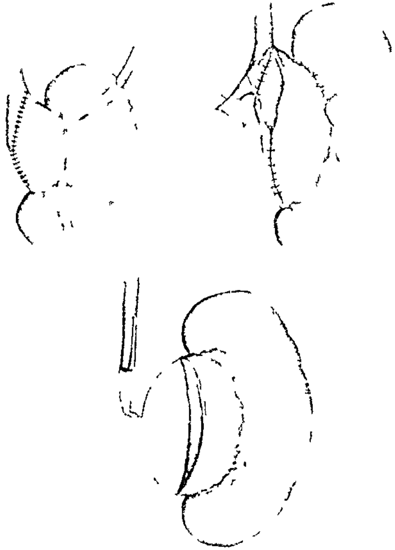

Fig 1 Method of resection of renal pelvis and ureteropelvic junction along with an stomosis

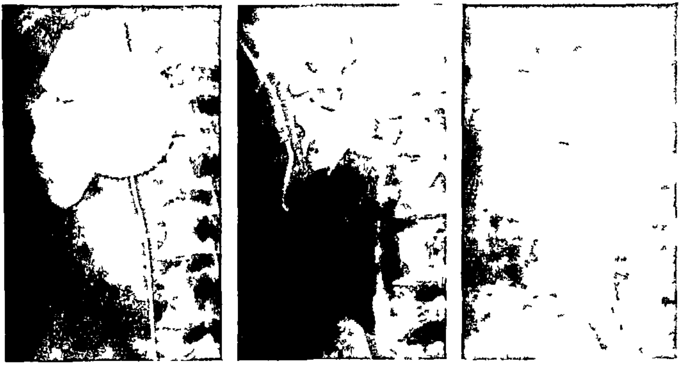

Fig 2 No 73086 A 27 year old man with massive hydronephrosis of solitary kidney and enal failure Second pyelogram shows patent ureteropelvic junction on seventh day follow ng surgery and final film demonstrates kidney 10 months later

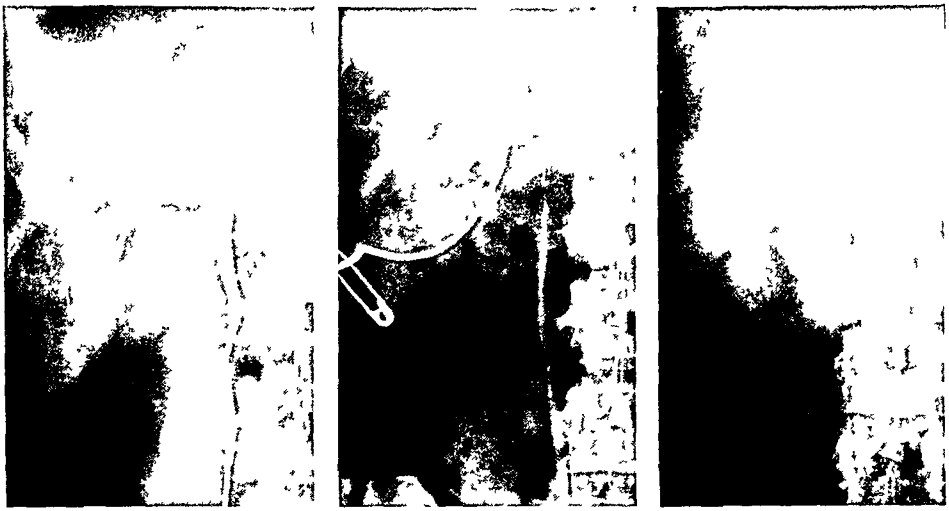

FIG. 3. No. 37133. A 47-year-old housewife with pyuria and nephrolithiasis Second film shows patency of ureteropelvic junction on fourth postoperative day Final film was taken 3 years later.

1) a ureteropelvic obstruction and 2) a dilated, decompensated renal pelvis. To correct the dilated renal pelvis by resection is inadequate unless the obstructed ureteropelvic junction is relieved. We prefer to remove the pathological process rather than to incorporate it in our repair and thus a resection of the redundant renal pelvis and ureteropelvic junction is employed.

Our procedure for the correction of pyelectasis is a simplification of the method described by Anderson and Hynes in 1949. The pelvis is cut off with scissors with a moderate curvature, the convexity of which faces the renal hilus (fig. 1). The ureter is severed as far below the ureteropelvic junction as possible and the proximal end of the ureter is split on its lateral aspect for 2 cm. A nephrostomy tube is inserted through the lower calyx. The cut edges of the ureter are sewn to

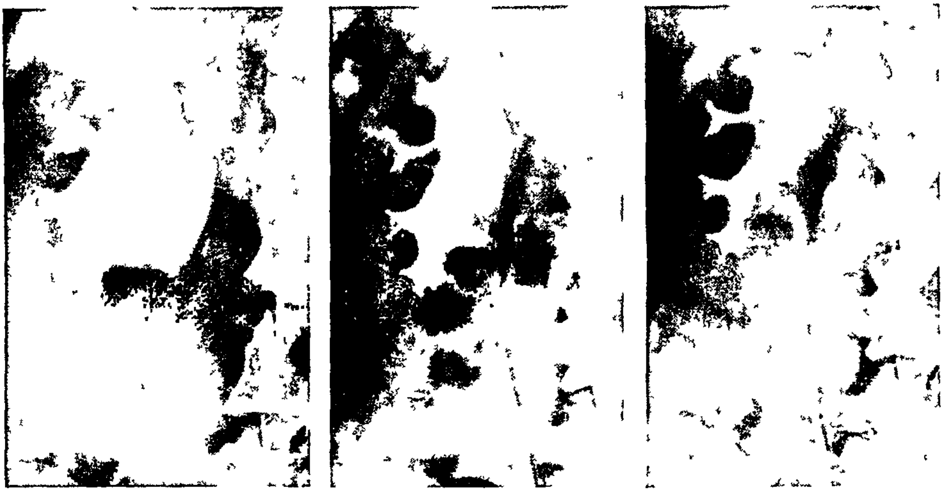

FIG 4 No 252775 A 37-year-old woman with infected hydronephrosis. First film is preoperative and following two films were taken 6 and 11 months following surgery.

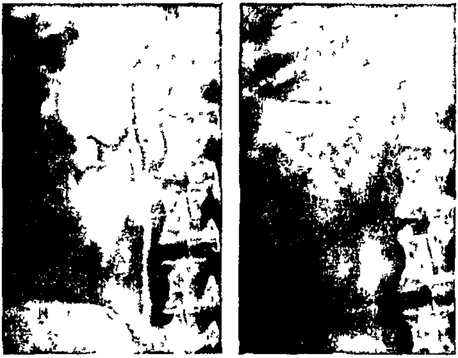

FIG. 5. No. 13937. A 44-year-old married woman with 10-year history of recurrent pyelonephritis First film is preoperative film showing congenital renal rotation with hydronephrosis Second film was taken 5 years following surgery during which time there had been no recurrence of urinary infection.

the edges of the renal pelvis after the upper portion of the pelvis has been approximated, as shown, using a continuous fine chromic suture. The wound is closed with a nephrostomy tube and drain emitting from its upper angle. The nephrostomy tube is removed on the seventh postoperative day along with the wound sutures. The drain is left in place until the eighth or ninth day. Usually by the ninth or tenth day the patient is permitted to leave the hospital. Full activity is permitted a month following surgery unless the patient is a laborer whereupon full activity is restricted for 6 to 8 weeks.

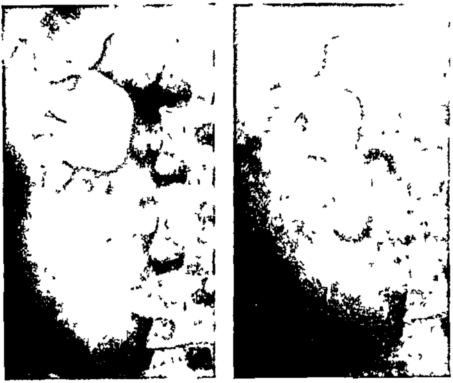

FIG 6 No 28790 A 19-year-old man with severely infected hydronephrosis First film is preoperative pyelogram, second one was taken 3 years later There has been no recurrence of symptoms in 5½ years during which time patient has been on active duty with U. S Marine Corps

Using this specific repair we have treated a total of 21 patients of whom 6 were operated upon by the resident staff of the Louisville General Hospital. The ages of these patients varied from 6 months to 52 years. The period of postoperative observation extends from 7 months to 5 years. The accompanying illustrations (figs. 2, 3, 4, 5, 6) serve as examples of our results.

In this group there have been two failures which we consider failures in judgment and not of the operation. One patient (a 20-year-old woman) demonstrated a massive pyelectasis with extremely poor function. Postoperatively she had severe pyelonephritis in the kidney that was operated on with increasing pyelectasis until nephrectomy was necessary. The ureteropelvic junction at the initial operation was markedly thickened with inflammatory reaction and at the time of nephrectomy it was inadequately healed and surrounded with marked fibrosis. The other patient who came to nephrectomy was a 48-year-old man in whom there existed extensive perinephritis and pyelonephritis. The repair failed due to poor healing at the anastomosis associated with extensive perinephritis and ureteritis. At nephrectomy the entire kidney and upper third of the ureter were encased in dense scar which of necessity was removed *en masse* without being able to identify the ureter until the specimen was dissected.

SUMMARY

The subject of ureteropelvic obstruction is discussed and the finding of ureteral valve-like structures in 9 of 15 specimens. A method of correcting ureteropelvic obstruction by resection of both renal pelvis and upper ureter is presented which has the advantages of surgical simplicity complemented by a short, comfortable convalescence.

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The Journal of Urology
Vol. 75, No. 1, January 1956
Printed in U.S.A.

PELVIC FUSED KIDNEY

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Fused pelvic kidney is one of the most unusual congenital anomalies encountered in urology, either clinically or at autopsy. It has been described variously as the lump, shield, cake, or discoid kidney since it presents as an irregularly-shaped fused pelvic mass. Reports of 11 cases can be found in the available literature. Kron and Meranze in a review of the literature to 1949 were able to find reports of 6 patients with this anomaly and reported an additional case. Baurys subsequently has reported two additional cases. Meredith Campbell in his textbook *Clinical Pediatric Urology* describes the anomaly in a 12-year-old girl and mentions a 19-year old boy with a severely infected pelvic lump kidney.

CASE REPORT

L. McK., a 24-year-old man, was well until November 1950, when he suffered an attack of mild periumbilical and suprapubic pain without associated gastrointestinal or genitourinary symptoms. On February 11, 1951, the same type of pain recurred, this time associated with *difficulty in initiating his urinary stream,* urgency and frequency, but no dysuria. At another hospital, a right lower quadrant mass was discovered. Catheterization relieved the pain but the mass recurred. He was admitted to this hospital on February 16, 1951. No further significant symptoms or past history could be elicited.

On physical examination a visible, nontender, firm, 12 to 15 cm. mass situated just above the pubis to the right of the midline was present. Rectal examination was negative.

Blood count, phenolsulfonphthalein test and urinalysis were within normal limits. The blood urea nitrogen concentration was 11 mg. per cent and a stained urinary sediment showed no abnormalities. No organisms grew in the urine culture. A flat film of the abdomen and x-ray of the chest were negative.

Excretory urograms showed contrast medium in the bony pelvic region only. Retrograde catheterization of the right kidney yielded 360 ml. of clear, sterile residual urine. The left kidney contained 30–40 ml. residual urine. Following pyelographic studies, the medium was withdrawn and the catheters were left indwelling for 24 hours, resulting in the prompt subsidence of the mass and the symptoms.

The pyelograms showed a huge right hydronephrosis, located at the brim of the pelvis, and a less severe hydronephrosis on the left (fig. 1). The ureteropelvic junction on the right could not be demonstrated, but the lower ureter appeared normal. A disc kidney was suspected because of the proximity of the pelves. The left ureteropelvic junction appeared somewhat narrow but was draining.

Accordingly on March 3, 1951, after induction of general anesthesia, the lower abdomen was prepared with ether and tincture of merthiolate, and draped. A right paramedian incision was made from the umbilicus to the pubis through the skin, subcutaneous tissue and anterior rectus sheath. All bleeders were

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Read at annual meeting, Southeastern Section of American Urological Association, New Orleans, La., March 20-24, 1955.

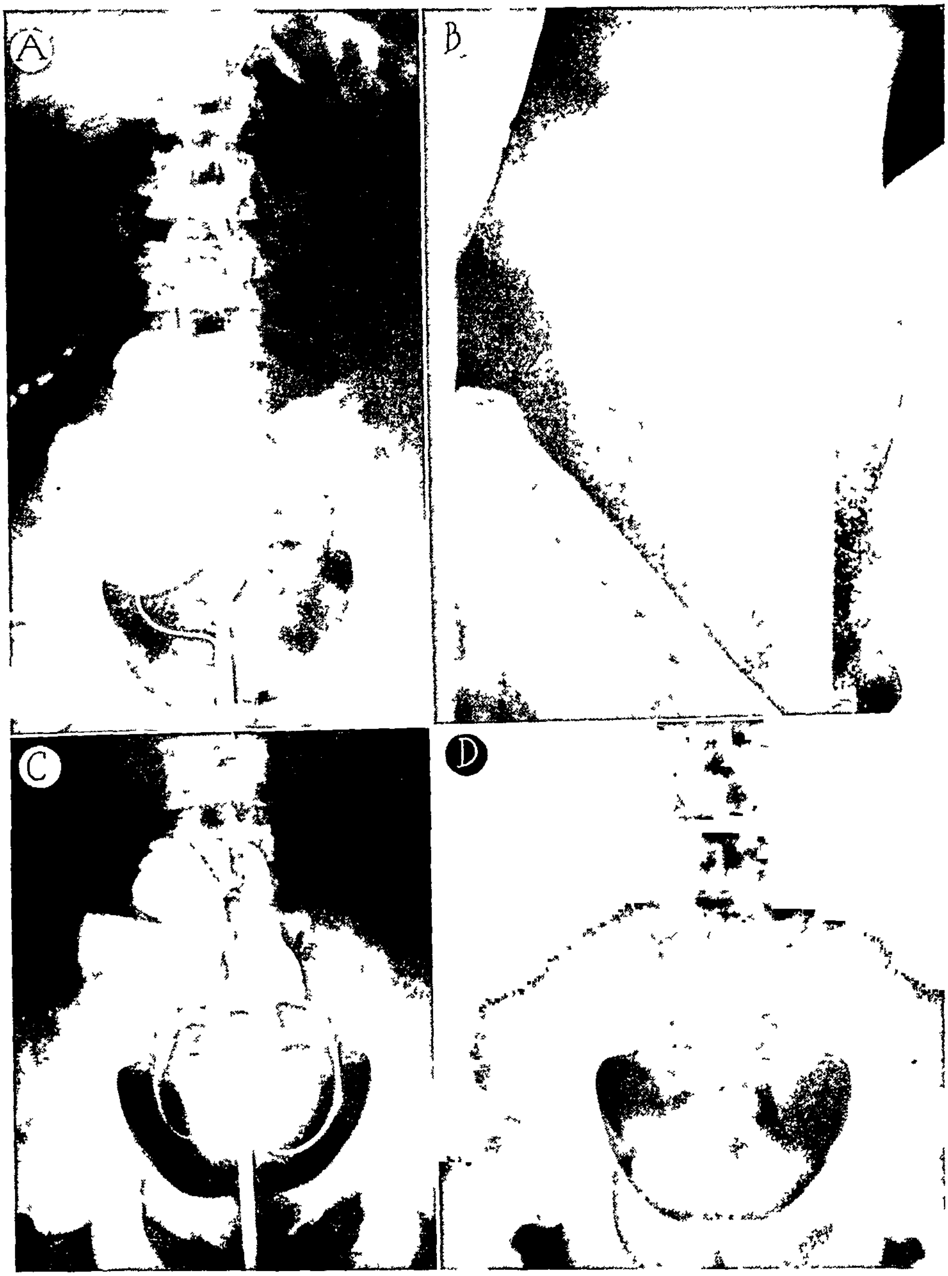

FIG 1 *A*, right retrograde pyelogram of pelvic fused kidney. Left pyelogram not available *B*, photograph showing visible mass *C*, retrograde pyelogram 4 months' postoperatively *D*, 45 minute delayed emptying film showing no evidence of stasis after complete filling of both pelves

clamped and ligated with plain 00 catgut. The rectus muscle was split along its fibers. The posterior rectus sheath was then opened exposing the peritoneum, which also was opened the entire length of the wound.

The patient was placed in a Trendelenburg position, and the bowel packed away revealing the hydronephrotic right renal pelvis. The posterior parietal peritoneum was incised longitudinally and by blunt dissection was separated from the pelvic kidney.

The right ureter was dissected free of numerous adhesive bands and found to enter the right renal pelvis in its middle third somewhat medially. Palpation showed that the right renal cortex composed about two thirds of the entire renal mass, whereas the left cortex composed only one third. The cortex was fused in the middle two thirds. The blood supply originated from the common iliac vessels. The left ureter was freed of adhesive bands and two small constricting blood vessels. Drainage of the left renal pelvis appeared satisfactory following this procedure. Attention was then directed to the right ureteropelvic junction.

It was thought necessary to place the ureteropelvic junction in a more dependent position and also to produce a larger lumen. A Y incision was then made through the right ureteropelvic junction. A stab wound was placed through the pelvis a short distance above the anticipated Y plasty and a 20F McIver nephrostomy inflatable catheter was inserted into the anteriorly situated right renal pelvis. The distal portion of the catheter was passed down the ureter to act as a splint. The apex of the pelvic flap was sutured into the lower end of the ureteral incision with atraumatic chromic 0000 catgut. The edges of ureter were then sutured to the edges of the defect in the renal pelvis with interrupted atraumatic chromic 0000 catgut, producing a much lower position and funneling of the right ureteropelvic junction.

The catheter was brought out through the lower aspect of the incision in a retroperitoneal position. The posterior parietal peritoneum was approximated with continuous suture of atraumatic chromic 00 catgut after a retroperitoneal Penrose drain had been inserted. A portion of small bowel mesentery was resected to prevent kinking of small bowel which may result subsequently because of suturing of the posterior parietal peritoneum.

The intestinal pack was removed and the peritoneum was closed. The rectus sheath was closed with interrupted chromic 00 catgut sutures. The subcutaneous tissue was closed with interrupted plain 00 catgut and the skin was closed with interrupted cotton mattress sutures.

The postoperative course was uneventful and the McIver splinting catheter was removed at the end of the third postoperative week. Excretory urograms at that time showed fair function with a marked decrease in the hydronephrosis. The patient was discharged on April 6, 1951. Four month followup excretory urograms (fig. 1) and supplemental retrograde pyeloureterograms (fig. 1) revealed marked improvement. The urine was infected with Alcaligenes faecalis which responded to gantrisin and terramycin. The urine cultures and sediment stains on additional visits remained negative and the patient continues to be free of symptoms.

DISCUSSION

Embryologically, it is believed that as the kidneys lie in the pelvic cavity, crowded together and incompletely isolated prior to passing the arterial fork, fusion may occur, thus producing the various forms of fused kidney.

The fused pelvic kidney is located over the sacral area or even lower. The pelves are usually located anteriorly with the bulk of cortex posteriorly, and the ureters most often enter the bladder in a normal position.

The diagnosis of renal ectopia is usually made by pyelography. The presence of a pelvic mass occasionally leads to the diagnosis, as in our case. Pain is a frequent presenting symptom and is thought to be due to the dragging or pulling on the vascular supply by the weight of the ectopic mass. Disease processes in such anomalous kidneys may be influenced by the blood supply and by the change in form and position of the pelvis, as well as by the location and course of the ureter. These render the patient more susceptible to urinary obstruction, infection and calculus formation.

A different plan of treatment will be necessary in each individual case depending on the patient's symptoms and whether or not obstruction, infection or calculus is present. Adequate drainage is the primary problem. In our case, this was successfully accomplished by a Y-plasty on the right and by simply freeing the ureter on the left since no other obstruction on that side was evident.

SUMMARY

A case report has been presented of a patient with a hydronephrotic fused pelvic kidney who thus far has had satisfactory results from a plastic repair of the ureteropelvic junction. In two postoperative examinations, the patient's kidneys have shown marked improvement, as evidenced by lack of infection, nonrecurrence of the hydronephrotic mass, improved pyelographic studies and absence of symptoms.

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The Journal of Urology
Vol 75 No 1 January 1956
Printed in U S A

OSTEOGENIC SARCOMA INVOLVING THE LEFT KIDNEY

HENRY C HUDSON

It is generally accepted that bone-forming metastases in the kidney are rare and primary osteogenic sarcoma of the kidney is extremely rare

A review of the literature reveals 5 cases which were reported as osteogenic sarcoma involving the kidney Weber,[1] in 1931, reported a case of osteochondrosarcoma of the left kidney and the left femur in a 15-year-old white girl These tumors were identical in structure, and he was unable to decide which was the primary site In 1936, Haming and Poole[2] reported a case of osteoblastoma of the left kidney histologically identical with osteogenic sarcoma This case was a 76-year-old man The tumor had metastasized to the right kidney, the liver, and the bowel Hamer and Wishard[3] reported a case of osteogenic sarcoma involving the right kidney in 1948 This case also was a 76 year-old man A case in which a transthoracic nephrectomy was done because of metastatic osteogenic sarcoma of the kidney was reported by Marshall and Drake[4] in 1950 Wilson,[5] in 1941, reported a case of extraskeletal osteogenic sarcoma in the mediastinum with metastases to the brain, the pancreas, the kidney, and the lungs in a 19-year-old man Only three of these were definite cases of extraskeletal osteogenic sarcoma

The case to be reported will be the sixth case on record of osteogenic sarcoma of the kidney

CASE REPORT

Mrs W C W , aged 52 (white), was admitted to the Carraway Methodist Hospital on October 13, 1953 She first noticed a mass in the left side of her upper abdomen in March 1952 In July 1952, she began having "stabbing pains" and soreness in the mass The tumor had progressively become larger During this 7-month period she lost 15 to 20 pounds in weight Ten days prior to admission she noticed total hematuria with clots This had cleared, however, in 2 days

The family history was negative for diabetes, tuberculosis, and cancer The past history revealed pyuria 5 years previously There were no symptoms referable to other systems of the body

Physical examination revealed blood pressure of 140/90 and temperature 98 6F Examination of ears, nose, throat, heart, lungs, and breasts revealed nothing abnormal Pelvic and rectal examinations were negative Palpation of the abdomen revealed a firm mass in the left upper quadrant which was the size of a large grapefruit This seemed to be attached to the posterior abdominal wall

Laboratory findings Kahn, negative Nonprotein nitrogen, 39 4 mg per cent

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Read at annual meeting, Southeastern Section of American Urological Association, New Orleans La March 20-24, 1955

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[5] Wilson H Ann Surg , **113** 95-112, 1941

Urinalysis: Specific gravity, 1.013; albumin and sugar, negative; microscopic, negative. Hemoglobin was 79 per cent (12.5 gm.); red blood cells, 3.6 million.

Sigmoidoscopy: negative. Chest x-ray: negative.

Cystoscopy revealed a normal bladder. A No. 6 catheter met an obstruction at 22 cm. in the left ureter; the right side was not catheterized because the kidney had been found to be normal by excretory urography. X-rays showed a large calcified mass in the upper left abdomen. After injection of shadowgraphic medium the pelvis and calyces were found to be moderately dilated and seemed to be above the mass. A lateral view gave the impression that the mass was anterior to and below the kidney and compressed the upper third of the ureter.

The patient was operated on October 17, 1952, through a transverse incision in the left upper abdomen using the transperitoneal approach. The left kidney and a portion of the transverse and descending colon were removed. The mass involved the lower pole of the kidney. It was moderately soft in some areas and bony hard in others. It was not attached to the spine or retroperitoneal muscles.

Pathological report: The specimen was a very large, irregular, hard mass of tissue which measured 16 by 14 by 11 cm. A 15 cm. segment of the colon was attached at one point. The tumor arose from the kidney. The outer surface of the tumor mass was very irregular. There were nodules projecting, some of which were very firm and hard with obvious calcification in them. Others were firm but contained no calcifications, while others were fluctuant and appeared cystic. The pelvis of the kidney was dilated and there was much soft, gray, necrotic-appearing material in the pelvis. Bone was encountered in the lower half of the specimen. This appeared to rise from the kidney itself. The ureter entered the upper portion of the pelvis and took a tortuous route over the surface of the tumor mass.

On section through the main tumor mass it was found to be composed mostly of bone with some fibrous components between the larger pieces of bone. In numerous areas there were large pieces of bone which were extremely hard and difficult to cut with the saw. Surrounding the entire tumor there was a very thin zone of compressed tissue which gave the appearance of a capsule.

Microscopic: In some regions, the tumor was composed of elongated, spindle-shaped cells which formed interlacing bands. These cells showed extreme variations in nuclear size and shape. There were many bizarre nuclear forms and many tumor giant cells. In other regions the structure of the tumor was somewhat different in that it was composed chiefly of bone. Sections through the kidney revealed fairly normal kidney tissue in some regions. Some of the tubules were filled with colloid-appearing material. There were many lymphocytes infiltrating the interstitial tissue. In other regions the kidney tissue had been chiefly replaced by tumor and in those regions one could find a few glomeruli completely surrounded by tumor tissue. Section in the region of the pelvis showed tumor tissue growing immediately adjacent to the pelvis. Diagnosis: Retroperitoneal osteogenic sarcoma with involvement of the left kidney (fig. 1).

A complete bone survey on November 4, 1952 yielded negative results.

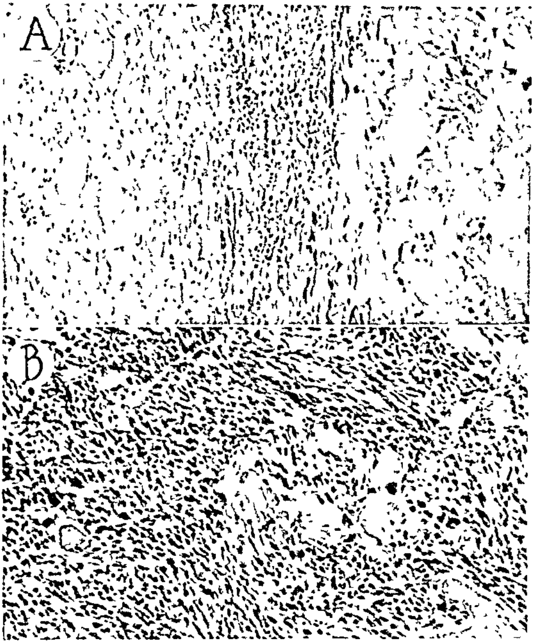

Fig. 1

The patient left the hospital on October 26, 1952. Her last clinic visit was on February 17, 1953. At that time a mass was present in the lateral end of the transverse abdominal scar. Another mass the size of a baseball was palpated in the left lower quadrant of the abdomen.

The patient died later at home. No autopsy was obtained.

DISCUSSION

The most plausible theory is that of metaplasia. It is thought that all bone arises from fibroblasts by a process of metaplasia. Under certain environmental conditions any connective tissue may revert to an embryonic state, and when this occurs, fibroblasts may become osteoblasts and form true bone. Other less likely theories are 1) occurrence of embryonic rests of osteogenic tumor misplaced during development which, in later years, due to changed physiological conditions, commence to grow and produce bone; 2) transference of osteoblasts by the blood stream to unusual locations.

Metastasis from a sarcoma reproduces its original cells more or less accurately, but it never produces bone unless its vascularity taps some supply of calcium such as bone or collection of calcium previously accumulated.

Calcification and ossification in soft tissue are not unusual pathological findings. These conditions occur in old hematomas, arteries, heart valves, pericardium, old tuberculous foci, and in old abdominal cicatrices. Ossification may occur in neoplasms having no skeletal connection. When the tumor is epithelial in origin, the bone is heteroplastic in nature, coming from connective tissue. By metaplasia the connective tissue cell may form bone; therefore, it is natural to assume that all types of bone tumors might occur in soft parts.

SUMMARY

Another case of osteogenic sarcoma of the kidney is reported.

A review of literature revealed only 5 cases of osteogenic sarcoma of the kidney. The case presented is a 52-year-old white woman.

Weber's case had sarcoma of the lower femur and of the kidney. He was unable to decide which was primary. Haining and Poole's case had metastasized to the other kidney, bowel, and liver. Hamer and Wishard's case had metastasized to the lung. At the time of the last study on my case, no metastases had occurred other than by local extension. The case is presumed to be primary osteogenic sarcoma of the kidney.

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The Journal of Urology
Vol 75 No 1 January 1956
Printed in U S A

OBSERVATIONS ON URETERAL OBSTRUCTION AND CONTRACTILITY IN MAN AND DOG

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Ureteral obstruction was probably first produced experimentally in animals by Galen[1] in the second century The nature and some of the characteristics of the contraction wave of the living ureter in animals were first described, in considerable detail, by Englemann[2] in 1869 Since that time and even earlier the peristaltic contraction of the ureter has been the object of repeated study and investigation Of particular interest to us is the attendant structural and functional changes in ureteral obstruction and contractility Furthermore, the management of the obstructed and dilated ureter is a problem frequently encountered in clinical urology, as pointed out by Hinman,[3] Campbell,[4] Charnock,[5] and many others Therefore, the following studies were undertaken

This preliminary report deals with varying degrees of ureteral obstruction as seen in patients and as produced experimentally in dogs The contractility of the dog ureter has been studied under conditions of moderate and severe obstruction In other experiments regeneration of the ureter, with and without obstruction, was allowed to proceed over a polyethylene tube either after a narrow ureteral strip was left in situ or after complete ureteral interruption The study of ureteral regeneration under various experimental conditions has been carried out by Kramer,[6] Wiseman,[7] Davis,[8] Weaver,[9] and many others Structural and functional changes in these ureters have been demonstrated by intravenous and retrograde pyelography and by cinefluorography (x-ray motion pictures) Struc-

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Read at annual meeting, American Urological Association, Los Angeles, Calif May 16–19, 1955

This study was supported with funds from a grant by the American Urological Research Foundation, Inc , the Adelina Ritter Shumway Research Fund, and the Department of Radiology

* This investigation was supported in part by a research grant (H 1192) from the National Heart Institute, of the National Institutes of Health, Public Health Service

The technical help of Mr Karl Sutter during the cinefluorographic studies is gratefully acknowledged

[1] *Galen on the Natural Faculties*, translated from the Greek by Arthur J Brock, M D , N Y , G P Putnam and Sons 1916 Bk I, chap 13, p 59

[2] Englemann, Th W Zur Physiologie des Ureter Pfluger's Arch f d ges Physiol , **2** 243–293, 1869

[3] Hinman, F The Principles and Practice of Urology Philadelphia W B Saunders Co , 1935, p 460

[4] Campbell, Meredith Clinical Pediatric Urology Philadelphia W B Saunders Co , 1951, chap 2 , p 103–158

[5] Charnock, D A Management of the dilated ureter J A M A , **157**. 574–576, 1955

[6] Kramer, S E Observations on rate of ureteral regeneration Surg , Gynec & Obst , **46** 216–220, 1928

[7] the stimulation influence of temporary rubber splitting on esection Brit J Urol , **6**· 11–26, 1934

[8] l Drake, W M Intubated ureterotomy Experimental wor **59** 851–862, 1948

[9] Weaver, R G and Henderson, J H Ureteral regeneration Experimental and clinical J Urol , **72** 350–357 1954

tural changes in the muscle and connective tissue of the ureteral wall were studied histologically in specimens stained by the Masson trichrome technique. In addition, segments of normal and abnormal human and dog ureters have been studied by a perfusion technique in which the effects of various drugs on the activity of ureteral muscle have been recorded under controlled conditions. Finally, since cholinesterase presumably plays a rôle in the transmission of the nerve impulse, and since neurological changes may be involved in some types of ureteral obstruction, this enzyme has been determined quantitatively in normal and abnormal ureters from patients and dogs.

METHODS

The dogs were given intravenous nembutal 25 mg. per kilo of body weight to produce anesthesia, and the surgical approach to the ureter was generally through the flank. The application of an aluminum band to the ureter to produce obstruction was usually near the ureterovesical juncture, while the regeneration studies involved the ureter near its juncture with the renal pelvis. The changes in the ureter under the above conditions were followed by intravenous pyelography using 70 per cent urokon,* 0.5 to 1 cc per kilo of body weight. In the retrograde studies a solution of 20 to 30 per cent urokon was injected through a 4 or 5F whistle tip ureteral catheter and either retrograde pyelograms were obtained or cinefluorographic studies were made.

In the ureteral regeneration studies a polyethylene tube 1.5 mm. in diameter and 5 to 8 cm. in length was used to bridge the defect, either in the complete ureteral interruption or in the regeneration from a strip of ureter (fig. 1, *B*). Silk ligatures held the tube in situ by being placed back of either bulbous part of the tube (fig. 1, *A*). These silk ligatures eventually cut through the ureter. The multiple openings at either end of the tube facilitate the flow of urine (fig. 1, *A*).

The cinefluorographic equipment used in these studies has been described elsewhere by Ramsey, et al.[10] The motion picture records were made on 35 mm. film, some at 7½ and some at 15 exposures per second. Henceforth the individual exposures will be referred to as "frames." Average x-ray factors were: 50 ma., 130 PKV, 1 mm. aluminum filtration, and target-to-screen distance 90 cm. In most cases two 20 second scenes were made of each animal, with a 10 or 20 second pause between scenes. X-ray dosage amounted to about 2 r per second measured at the near point of the skin. The dogs, which weighed between 30 and 40 pounds, were placed in front of the fluorographic screen during a preliminary fluoroscopy.

CLINICAL STUDIES

Ureteral obstruction in the human can be, indeed, extremely severe and yet through suitable clinical management marked improvement in appearance and function can be attained as demonstrated in the following 3 patients.

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* Urokon used in these studies was generously supplied by Mallinckrodt Chemical Works, St. Louis, Mo.

[10] Ramsey, G. H. S., Watson, J. S., Jr., Steinhausen, T. B., Thompson, J. J., Dreisinger, F. and Weinberg, S.: Cinefluorography. Radiology, **52**: 684–690, 1949.

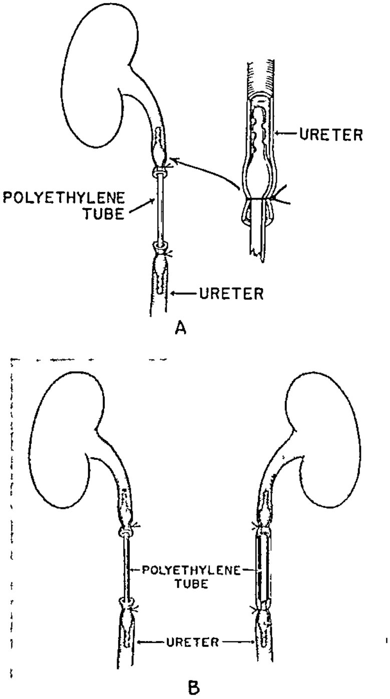

FIG. 1. *A* and *B*, polyethylene tube used to bridge ureteral defects. Multiple perforations in tube permit urine to flow through tube, pass defect, and down distal ureter.

D. A. (SMH; 248470) was first seen at the age of 5 years with bladder neck obstruction, spina bifida, and very marked vesicoureteral reflux (fig. 2, *A*). After suprapubic catheter drainage for 7 years one can see the complete disappearance of left vesicoureteral reflux (fig. 2, *B*) and marked improvement in the appearance of the right ureter and kidney.

C. C. (SMH; 292516) aged 5 months had marked ureteral obstruction and dilatation of double left ureter and pelvis. The drawing (fig. 3, *A*), summarizes the pyelographic findings in this infant. An upper left heminephrectomy and complete ureterectomy were performed to remove marked hydronephrosis and hydroureter as shown in figure 3, *B*. In addition, resection of 6 cm. of the remaining redundant ureter with an oblique end-to-end anastomosis was carried out according to the method of Boveé[11] and Hinman.[12] The result of this operative

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[11] Boveé, J. W.: Ureteroureteral anastomosis. Ann. Surg., **25:** 51–70, 1897.

[12] Hinman, F.: Obstructive hydroureteral angularity with hydronephrosis in children. Arch. Surg., **18:** 30–62, 1929.

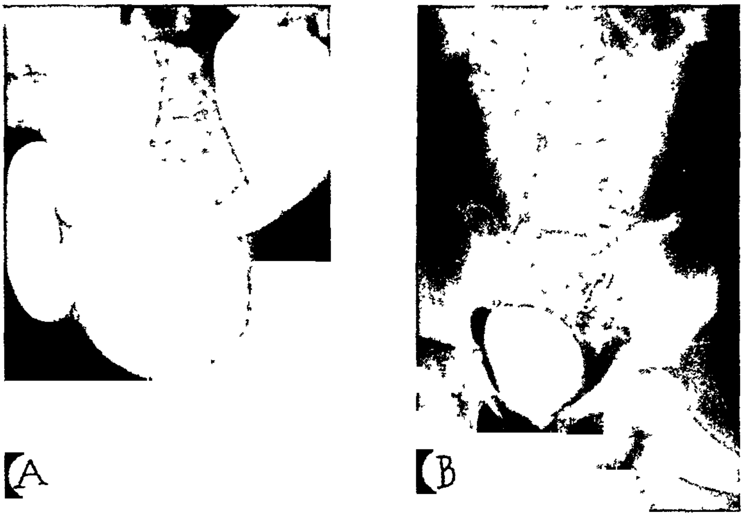

Fig. 2. D. A. (SMH; 248470). *A*, cystogram demonstrates strikingly vesicoureteral reflux and bilateral ureteral elongation, kinking, and enlargement. *B*, cystogram shows result of 7 years of suprapubic drainage of bladder and marked reduction in size of right ureter as well as diminution in ureteral kinking and elongation. Note absence of left vesicoureteral reflux and presence of spina bifida.

procedure is shown in figure 3, *D* (note lower ureter size; arrow). One of the periureteral bands which is shown in figure 3, *C* was associated with the kinking and obstruction as pointed out by Benjamin and Tobin.[13] Periureteral bands associated with an inflammatory condition and ureteral obstruction have been described by Ormond[14] and Bradfield,[15] but there was no evidence of an inflammatory reaction in these periureteral bands.

S. T. (SMH; 382623) was first seen at the age of 5 years with a double left ureter and pelvis. The upper pelvis and ureter were markedly dilated. This enlargement started at the ureterovesical juncture, at which site the ureter became very narrow for a distance of about 1 cm. Histological preparation of the removed narrowed ureter, when stained by the Masson trichrome method, revealed that it was essentially a fibrous structure, and almost devoid of muscle fibers (fig. 4, *B*); whereas the dilated ureter, which was similarly treated, showed an increase in the amount of connective tissue and smooth muscle (fig. 4, *A*; arrows). In some respects the aforementioned findings simulated our findings in the dog, when obstruction was produced by the application of an aluminum band to the ureter near its juncture with the bladder. Subsequently, as a result of obstruction, the ureter showed enlargement and increase in the amount of connective tissue and of smooth muscle as seen in figure 12.

In the dog, the result of left ureteral obstruction and the attendant elongation enlargement is shown in figure 5, *B* to *E*, which can be compared to the normal

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[13] Benjamin, J. A. and Tobin, C. E.: Abnormalities of the kidneys, ureters, and perinephric fascia: Anatomic and clinical study. J. Urol., **65**: 715–731, 1951.

[14] Ormond, J. K.: Bilateral ureteral obstruction due to envelopment and compression by an inflammatory retroperitoneal process. J. Urol., **59**: 1072–1079, 1948.

[15] Bradfield, E. O.: Bilateral ureteral obstruction due to envelopment and compression by an inflammatory retroperitoneal process. J. Urol., **69**: 769–773, 1953.

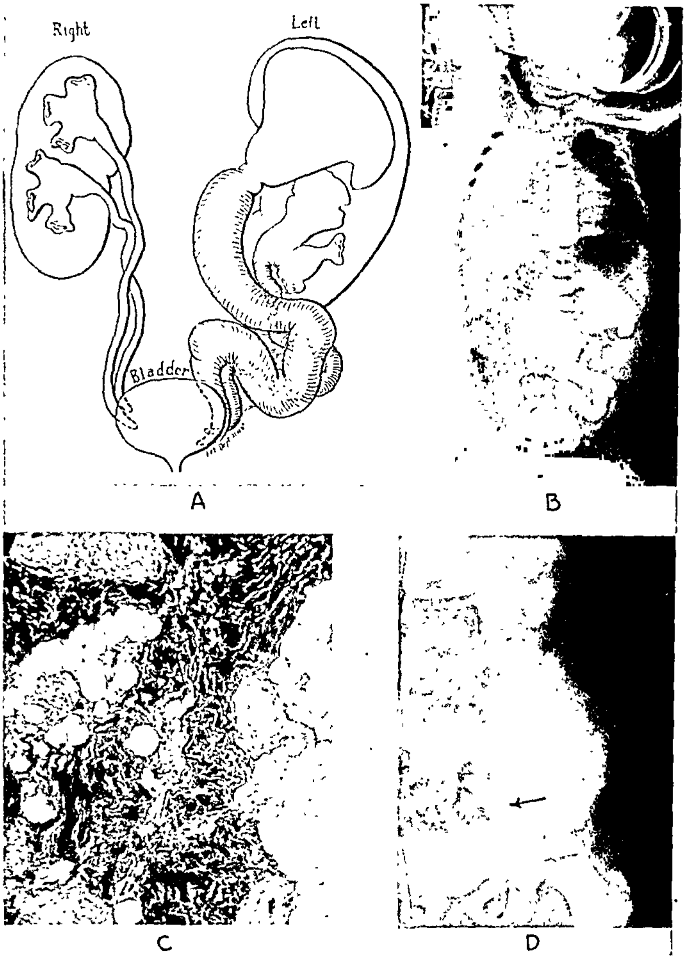

Fig. 3. C. C. (SMH; 292516). *A*, drawing to reconstruct findings obtained from retrograde pyelography at age of 5 months. *B*, retrograde pyelogram of upper left ureter which is dilated, elongated, and has multiple angulations. This ureter and a portion of the kidney were removed. *C*, portion of periureteral band to demonstrate blood vessels and increased connective tissue which was associated with ureteral obstruction. *D*, three years later, result of heminephrectomy of upper left kidney and complete removal of ureter. In addition, 6 cm. mid-ureteral resection of remaining ureter and oblique end-to-end anastomosis were carried out. Note ureteral growth maintained pace with body growth. Arrow points to lower ureter.

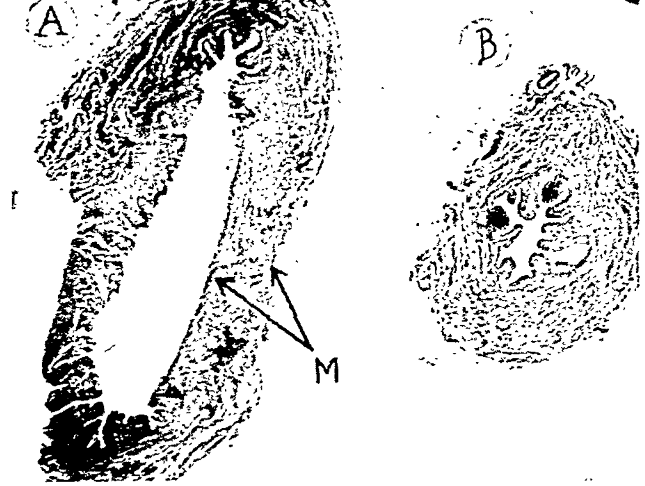

FIG. 4. *A* and *B*, transverse section through ureter to demonstrate that the portion near ureterovesical juncture was mainly fibrous tissue (*B*). Narrowing of ureteral lumen at this site produced obstruction, marked enlargement, and increase in amount of smooth muscle (*A*; arrow M) (×7.5).

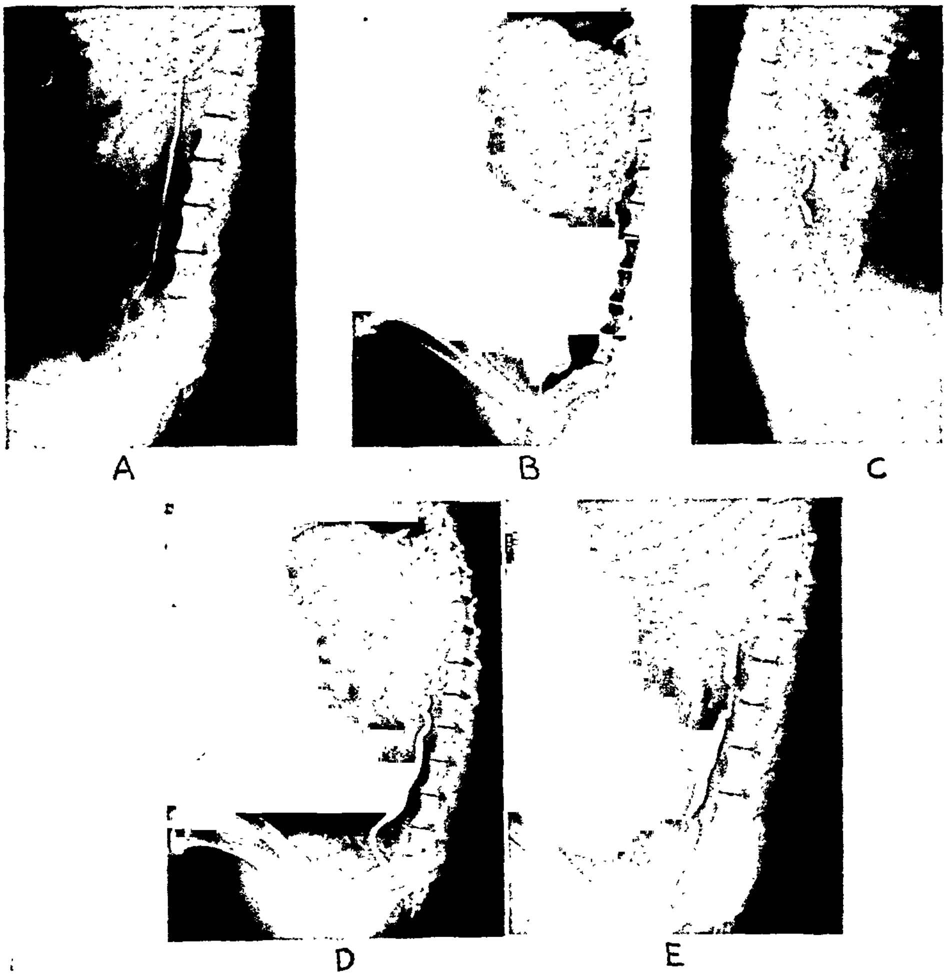

FIG. 5. *A*, retrograde pyelogram showing normal dog ureter. *B* and *C*, retrograde pyelograms of moderately dilated dog ureters demonstrating early dilatation and beginning elongation as result of lower and upper ureteral obstruction. *D* and *E*, retrograde pyelograms showing more dilated, kinked, and elongated ureters as a result of obstruction at ureterovesical junction.

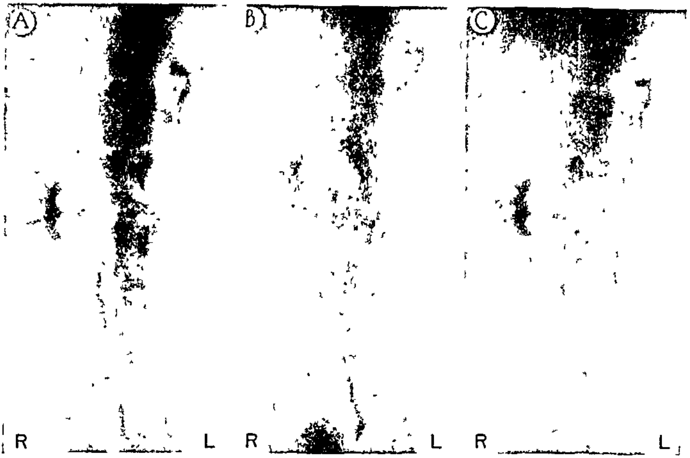

FIG. 6. Contraction waves in normal dog ureter, shown on selected frame of x-ray motion picture film. *A*, contraction waves beginning in upper third of right ureter. *B*, first wave spreads downward, while a second wave begins at ureteropelvic junction *C*, contrast medium has been expelled from most of ureter, but residue remains in renal pelvis

left ureter (fig. 5, *A*). The degree of obstruction seen in figure 5, *B* was produced in 3 weeks by applying an aluminum band loosely at the ureterovesical juncture. When moderate obstruction was produced, in the same manner as previously stated, in the upper ureter (fig. 5, *C*) it became dilated, elongated, and kinked. The degree of ureteral obstruction and resultant hypertrophy, elongation and angularity can be increased by permitting the obstruction to proceed slowly over a period of 3 to 4 months (fig. 5, *D* and *E*).

CINEFLUOROGRAPHY

After retrograde filling of the ureter, pelvis, and calyces of a normal dog with 30 per cent urokon, ureteral contractions are seen to begin at the ureteropelvic junction (fig. 6, *B* and *C*). The contrast medium is returned from the kidney pelvis to the ureter in quick, intermittent spurts or jets. Ureteral contraction waves, forceful enough to obliterate the lumen, then sweep down the ureter to the bladder. In some cases the traveling contraction is only a few centimeters in length (fig 6, *A*), and the lumen opens up again behind it, apparently in response to a second ejection of contrast medium from the kidney pelvis. In other cases the entire length of the ureter may remain contracted below the advancing wave front, so that nearly all the contents of the ureter are expelled (fig. 6, *B* and *C*). Residual medium is seen remaining in the pelvis and calyces. The absence of the contrast medium in the ureter, at the site of contractions, gave evidence that the peristaltic waves are sufficiently forceful to obliterate the lumen. There was no evidence in these studies that the normal dog ureter was dilated, elongated, or enlarged during the contraction movements of the ureter, or that

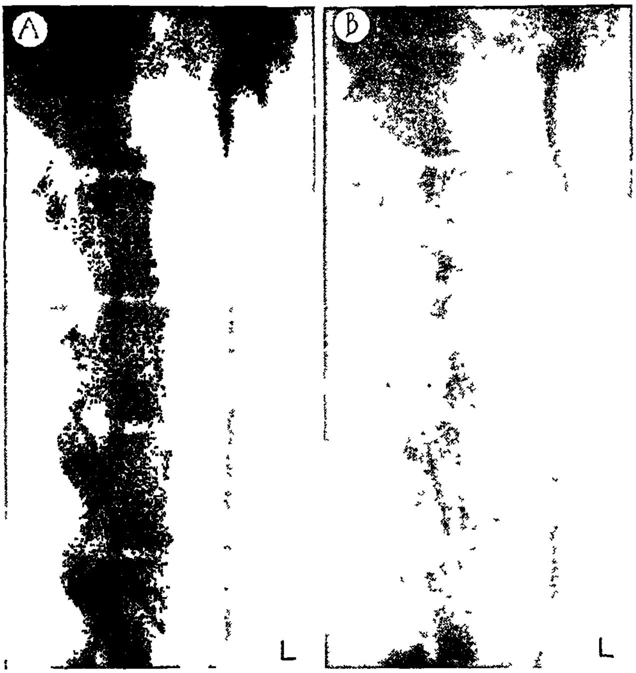

FIG. 7. Contraction of moderately dilated ureter, which has been obstructed at ureterovesical junction by an aluminum band. *A*, early widening and elongation of obstructed left ureter near ureteropelvic junction. *B*, contraction of middle portion of the ureter resembles one seen in figure 6, *B*.

the catheter produced abnormal contraction waves. Wislocki and O'Conor[16] found no abnormal ureteral contraction waves when they injected Locke's solution by catheter into the normal ureter of 4 dogs. However, if the ureter was markedly distended, then peristaltic waves may entirely stop.

When the ureter was minimally obstructed by placing an aluminum band near the ureterovesical juncture, moderate ureteral enlargement, elongation and kinking could be produced (fig. 7, *A*). The elongation and bending usually, under these conditions, developed near the ureteropelvic juncture. The contraction waves, however, are quite similar to those of the normal ureter just described (fig. 6, *B*). In this instance the wave was long, appeared pinched off at either end; and again, as in the normal ureter, the medium at the site of contraction was completely removed from the ureteral lumen. If the obstruction was more severe the dilatation, elongation, and angularity were correspondingly increased. When the ureter is markedly distended as a result of obstruction then one may not see contraction waves during cinefluorography, or else the waves will be short (fig. 11) and sluggish, as seen in the x-ray motion pictures.

In these experiments one half of the circumference of the ureter has been removed for a distance of 5 cm. and the defect bridged by a polyethylene tube as shown in figure 1, *B*. The ureter was then allowed to regenerate over this tube and 5 months later this x-ray motion picture was made. Active ureteral contrac-

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[16] Wislocki, G. B. and O'Conor, V. J.: Experimental observations upon the ureters with especial reference to peristalsis and antiperistalsis. J. H. H. Bull., **31**: 197–209, 1920.

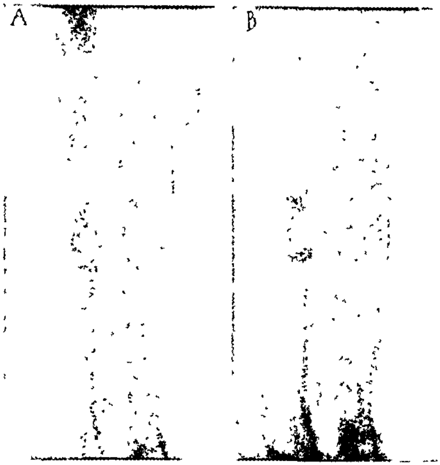

FIG. 8. Contractions of regenerating strip of ureter. *A*, one-half of circumference of left ureter has been removed for a distance of 5 cm. and remaining ureteral tissue allowed to regenerate over a polyethylene tube. A diverticulum has developed at site of regeneration between two silver clips (indicated by arrows). *B*, active contractions above and below defect are better demonstrated in x-ray motion picture This single frame shows ureteral contractions similar to those seen in normal ureter in figure 6, *B*, except these are shorter in length. Diverticulum has no tendency to contract or empty itself of contrast medium.

tions are seen in the x-ray motion picture above and below the ureteral regenerating site marked by 2 silver clips (fig. 8, *A* and *B*; arrows). In fact these are similar to the normal and moderately dilated ureter contraction waves, except they may be slightly shorter. The contraction waves above and below the defect did not appear to be in sequence or synchronous. Of interest was the development of a diverticulum (fig. 8) at the site of ureteral regeneration. In the study of the frames composing the x-ray motion picture there was no evidence that the diverticulum could contract; however, a flat film of the abdomen the next day showed no evidence of medium at this site, indicating probable drainage by gravity flow. A cross section of the diverticulum provided an explanation for the noncontractility because it was essentially a fibrous sac devoid of muscle fibers (fig. 9, *A*); whereas smooth muscle was found in the regenerating portion of the ureter (fig. 9, *B*).

In these experiments the ureter has been completely excised for a distance of 5 cm. and the defect bridged by polyethylene tube as shown in figure 1. Above the upper silver clip marked by an arrow there was a little dilatation of the ureter while below the lower silver clip (arrow) the ureter appeared near normal in size. Again, as in the previous regeneration experiment in which a strip of ureter was left, the contraction waves were seen both above and below the ureteral defect. These waves did not appear to follow in sequence or to be synchronous. These scenes cover a total of 40 seconds, and perhaps longer periods

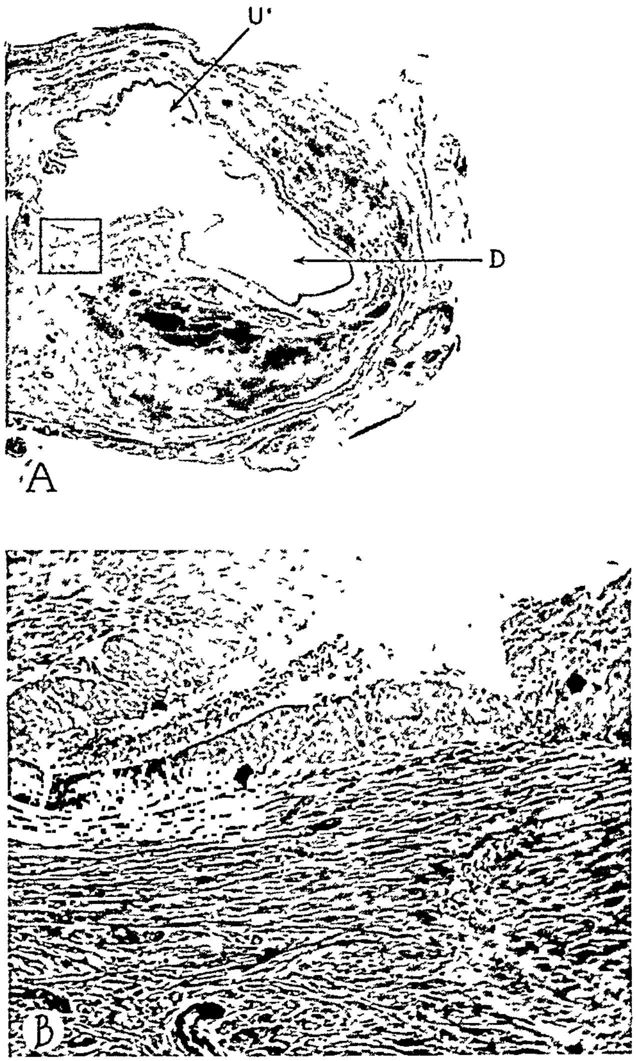

FIG. 9. *A*, transverse section through regenerating ureter and diverticulum. Muscle tissue is almost absent from diverticulum and appears to be poorly organized in regenerating portion of ureter. (×10) (*U*, ureter and *D*, diverticulum). *B*, magnified portion of regenerating ureter from square in (*A*) to show increased epithelization and fibrous appearance of ureteral wall (×150).

of time are required to determine if the waves above and below are in sequence. There was a churning or regurgitation action noticeable in the x-ray motion picture and this may be partly related to the resistance to flow of urine through the small polyethylene tube which is 1.5 mm. in diameter. Of interest was the ureteral dilatation (fig. 10, *A*; upper arrow) which disappeared after ureteral contraction (fig. 10, *B*; upper arrow).

When the ureter was completely interrupted, the site of which is marked by 2 arrows in figure 11, and then allowed to regenerate over a polyethylene tube for a period of 6 months the following studies were made. Obstruction of the ureter was then produced at the ureterovesical juncture by applying an aluminum band

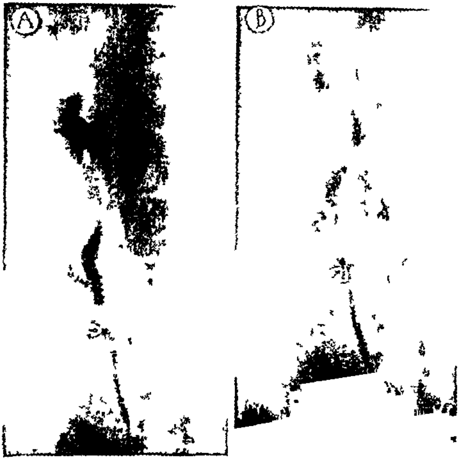

Fig 10 Contraction of completely interrupted regenerating ureter *A*, note local dilatation of ureteral lumen just above upper silver clip (arrow) Contractions in upper intact portion of ureter are similar in appearance to those seen in figure 6 *B* *B*, dilation of lumen above defect is now less noticeable (upper arrow) Active contractions taking place below defect are well demonstrated in x ray motion pictures

Fig 11 Contraction wave of completely interrupted regenerating ureter which is also moderately dilated Left ureter has been completely interrupted for distance of 5 cm, marked off by two silver clips (arrows) Defect has been bridged with polyethylene tube Note square cut off appearance at either end of contraction wave in intact upper ureter (upper arrow)

moderately tight and within 2 months there was elongation and dilatation of the ureter. At this time the contraction wave was short, rather squarely cut off at either end and the movement of the ureter was limited to the region near the ureteropelvic juncture as shown in figure 11 (upper arrow). There appeared to be no activity in the ureter below the defect, at least not for the 40 seconds that cinefluorographic observations were made. If longer periods of time were available for x-ray motion pictures the findings might be changed.

HISTOLOGY

Histological preparations were stained by the Masson trichrome method, which facilitates the identification of muscular and fibrous components of the ureteral wall. In ureters chronically dilated as a result of partial occlusion, the enlargement involved not only an increase in diameter of the ureter but also an increase in amount of smooth muscle (figs. 12 and 13). The increase was symmetrical and without apparent distortion of the arrangement of the muscle bundles. Hryntschak[17] and Boyarsky[18] found, as we did, that the smooth muscle in the regenerating ureter did not establish normal appearing architecture (fig. 9, *B*). The question of the extent to which proliferation and hypertrophy of smooth muscle fibers contribute to the increase in muscle mass requires further study.

PERFUSION STUDIES

The perfusion apparatus used in the studies has been described in detail elsewhere by Emmel and Smith.[19] The essential principle is that during perfusion the specimen is contained in this, a closed, rigid, fluid-filled system, which is in communication with a sensitive electrical pressure transducer. Under these circumstances contraction of the ureteral wall produces no appreciable narrowing of the lumen, but does produce a reduction in pressure within the fluid surrounding the specimen. It is this reduction in external pressure which is measured and recorded. The muscular contraction here is isometric.

Specimens for study are 1 to 2 cm. long. A specimen is first carefully cleaned of surrounding fat and connective tissue. It is then turned inside out, tied between cannulae and inserted in the perfusion chamber. The perfusate is a modified Locke's solution aerated with O_2 and CO_2 (95:5) to give a pH of 7.2–7.4. Temperature is maintained at 37C. Substances to which the reactivity of ureteral muscle is being tested are injected into the perfusion line and carried through the specimen with the flow of perfusate.

The response of ureteral muscle to a variety of chemical agents will be described in detail in another communication. The comments here will be limited to the results obtained with histamine. Test doses were 0.05 ml. of a 1:1000 solution of histamine phosphate. During passage through the specimen this repre-

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[17] Hryntschak, Th.: Zur Histologie and Physiologie des querdurchtrennten Harnleiters. Ztschr. f. urol. Chir. u. Gynäk., **42:** 268–291, 1936.

[18] Boyarsky, Saul and Duque, Oscar: Ureteral regeneration in dogs: an experimental study bearing on the Davis intubated ureterotomy. J. Urol., **73:** 53–61, 1955.

[19] Emmel, V. M. and Smith, D. J.: Pressure measurements in perfused segments of small blood vessels. Proc. Soc. Exper. Biol. & Med., **78:** 561–562, 1951.

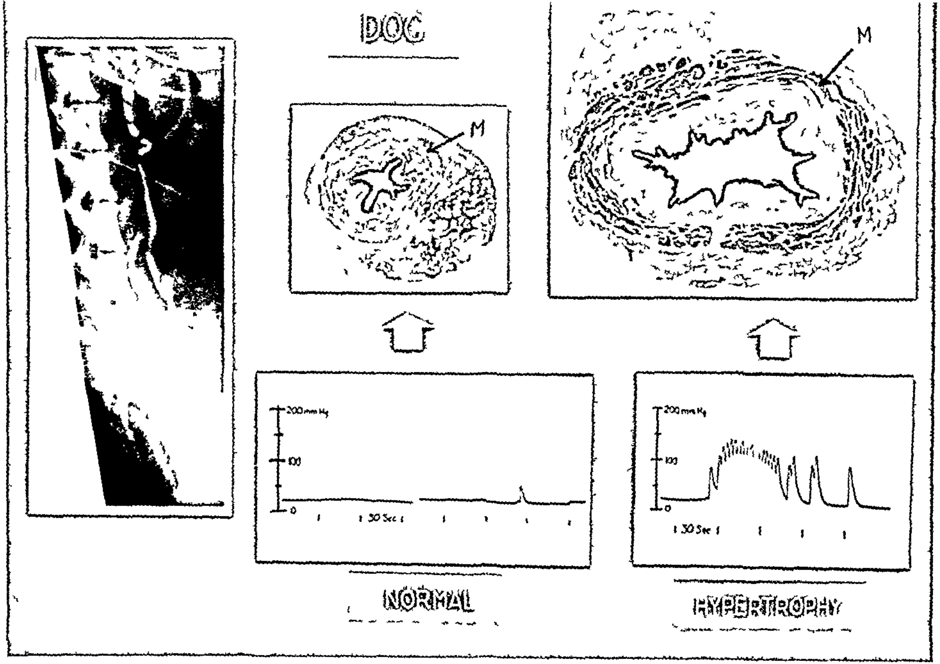

Fig 12 Summary of the findings in a normal and an obstructed dog ureter *A*, retrograde pyelogram showing obstruction near ureterovesical juncture produced by an aluminum band Ureter is enlarged and elongated *B*, transverse section of normal dog ureter in which arrow M points to smooth muscle *C*, record of contractions of normal ureter in response to 50 gamma of histamine *D*, transverse section of obstructed and hypertrophied ureter Increase in both connective tissue and smooth muscle (arrow M) is present *E*, shows pressure response of ureter in perfusion chamber to 50 gamma of histamine Marked activity is shown by this specimen

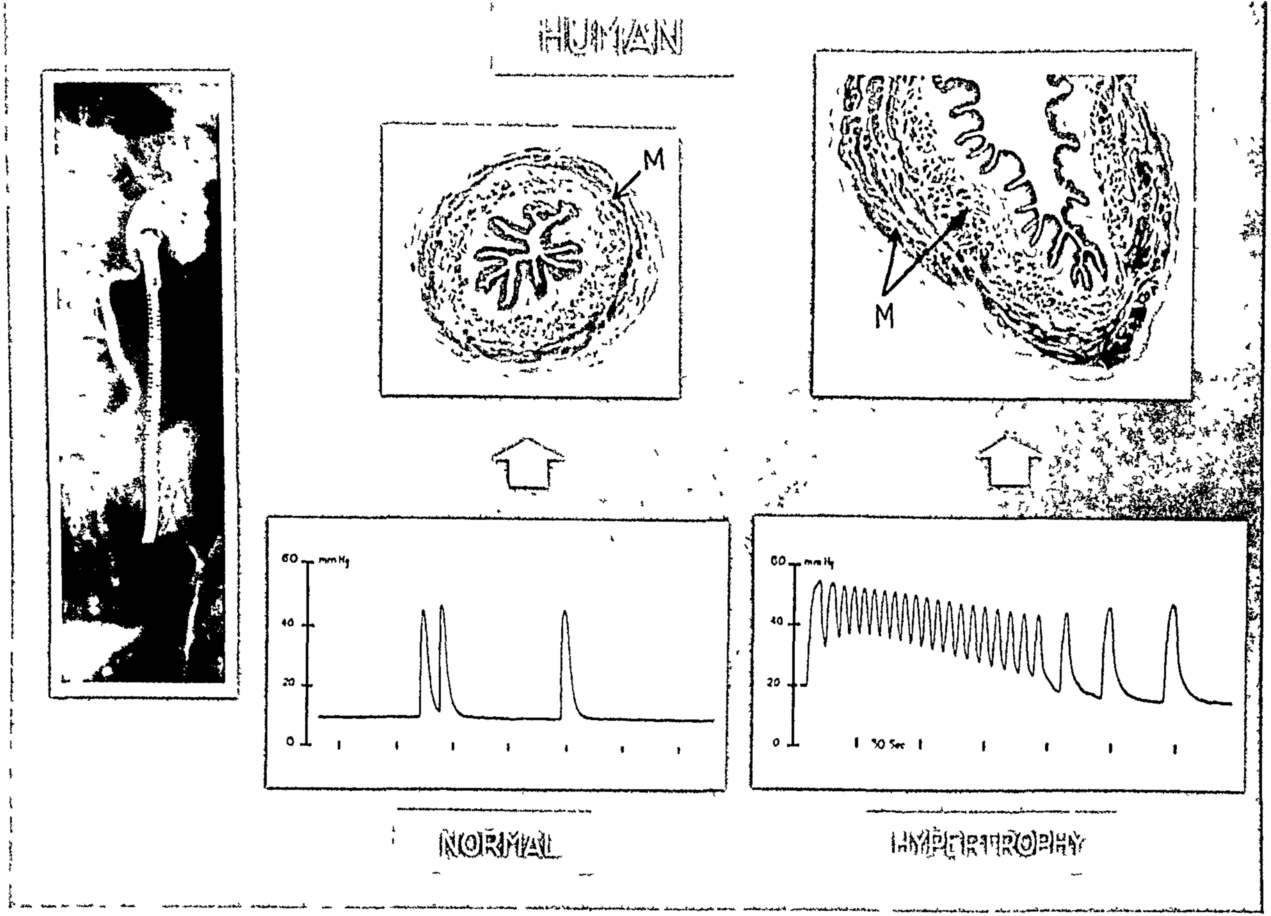

FIG. 13. Summary of findings in normal and obstructed human ureter. *A*, retrograde pyelogram showing obstruction near ureterovesical juncture produced by scar tissue. Ureter is enlarged and elongated. *B*, transverse section of normal human ureter in which arrow M points to smooth muscle. *C*, record of contractions of normal ureter in response to 50 gamma of histamine. *D*, transverse section of obstructed and hypertrophied ureter. Increase in both connective tissue and smooth muscle (arrows M) is present. *E*, shows pressure response of ureter in perfusion chamber to 50 gamma of histamine. Marked activity is shown by this specimen.

sented a transient maximum intralumenal concentration of 50×7 histamine per ml.

OBSERVATIONS

The normal dog ureters and the few presumably normal human specimens which were studied showed no spontaneous activity and gave only slight or inconstant responses when stimulated with histamine (figs. 12 and 13). The hypertrophied and dilated specimens, however, responded vigorously to this substance (figs. 12 and 13). The response characteristically consisted of a patterned sequence of rapid contractions which tended to merge, thereby producing a sustained but fluctuating general increase in muscle tone. This gradually subsided as the contractions became individualized, less frequent and finally ceased. Pressures developed by the dog specimens were as much as 100–150 mm. Hg, while the human specimens (2) produced pressures of approximately 60 mm. Hg. It should be mentioned that in terms of physiological state, the human specimens may not be exactly comparable to those from the dogs, since the former were subjected to more extensive operative manipulation prior to perfusion.

Normal ureteral segments observed during perfusion without previous specific chemical stimulation generally showed no spontaneous activity. However, several of the chronically dilated dog ureters, after having responded several times to histamine, developed rhythmic transient individual contractions occurring at intervals of about 30 seconds and continuing for 20 to 30 minutes.

The above observations indicate that the smooth muscle in the wall of an enlarged ureter is not only increased in amount, but also that it is in an altered state of reactivity. The nature and significance of this alteration are being investigated.

ENZYME STUDIES

Cholinesterase studies were designed to establish whether the ureteral enzyme was of the specific or nonspecific type and to determine whether there was a quantitative difference in enzyme activity between normal and dilated ureters.

Cholinesterase activity was determined using the manometric method described by Ammon,[20] in which the hydrolysis of the choline ester is followed by measuring the evolution of carbon dioxide from a carbon dioxide bicarbonate buffer system. The measurements were carried out at 37C and pH 7.4. For the specificity studies the following substrates were employed at 4×10^{-3} M concentrations, acetyl choline chloride, propionyl choline p toluene sulfonate,* butyryl choline p toluene sulfonate,* benzoyl choline chloride and acetyl betamethyl choline chloride (mecholyl). Cell-free 5 per cent homogenates of ureter were prepared in Krebs Ringer's bicarbonate solution. The nitrogen content of the homogenates was approximately 1 mg./ml. Each Warburg flask contained the choline ester, 1.0 ml. of homogenate, 0.5 per cent gelatine, and sufficient Krebs

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[20] Ammon, R. Die fermentative Spaltung des Acetylcholins. Pfluger's Arch. f. d. ges. Physiologie, 233: 486–491, 1933.

* We are grateful to Dr. J. A. Aeschleman of Hoffman LaRoche Inc., Nutley, New Jersey for generously making butyryl choline p toluene sulfonate and propionyl choline p toluene sulfonate available to us.

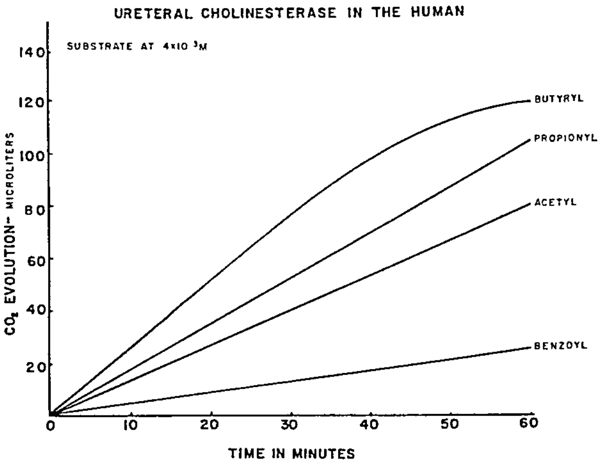

FIG. 14. Choline ester hydrolysis is plotted as ordinate (carbon dioxide evolution in microliters). Time is plotted as abscissa.

Ringer's bicarbonate solution to give a final volume of 3.2 ml. The results are shown in figure 14. The butyryl choline was hydrolyzed most rapidly. The rate of hydrolysis of propionyl choline was between that of butyryl and acetyl choline. According to the criteria for determining the specificity of the enzyme outline by Augustinsson,[21] these substrate-activity relationships indicate that the cholinesterase of the ureter is of the nonspecific or pseudo-cholinesterase type. Further evidence for this stems from the fact that benzoyl choline was hydrolyzed by the ureteral preparation, while mecholyl was not. This pattern of activity has been observed in both man and the dog.

Applying a histochemical technique to the dog ureter, deKlerk[22] reached a similar conclusion. Our data with cell-free homogenates allow a quantitative evaluation of ureteral cholinesterase and provide a conclusive demonstration that the enzyme is nonspecific.

It is considered important to determine whether the cholinesterase activity of normal and pathological ureters differed quantitatively. Acetylcholine chloride, at 6×10^{-3}M concentration, was used as substrate for this assay. When less than 1 ml. of 5 per cent homogenate was used, it was found that the velocity of acetyl choline hydrolysis was proportional to the amount of homogenate added. Specimens were assayed at 2 or 3 levels of homogenate. The results are shown in table 1. With human ureters, there were no differences in the average activities of the normal and pathological groups. The human ureter was found to be much less active than the dog ureter. With two dog ureters which were experimentally dilated (not shown in table 1) the cholinesterase level was found to fall within the normal range for the dog. Thus there appeared to be no differences in cholinesterase activity between normal and pathological ureters. However, there

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[21] Augustinsson, Klas-Bertil: The Enzymes. Acetylcholine. Esterase and Cholinesterase. Academic Press, N. Y., 1950, vol. 1, pt. I, chap. 10, p. 443.

[22] deKlerk, J. N.: Type and distribution of choline esterases of urinary collecting system of dog: their relationships to ureteral pertussis and possible role in congenital anomalies. J. Urol., 72: 787–798, 1954.

TABLE 1 *Cholinesterase activity of cell free homogenates of ureter from various species*

Species and Condition	Number of Experiments	μMoles Acetylcholine hydrolyzed per hour per mg Nitrogen	
		Average	Range
Human—Normal	18	2.7 ± 0.9*	1.9–4.2
Human—Dilated	9	2.5 ± 1.3*	1.3–4.2
Dog—Normal	7	7.9 ± 3.7*	6.0–10.0
Rabbit—Normal	3	4.7	4.5–5.0

* Standard Deviation

appeared to be a significant difference in the amount of ester hydrolyzing ability of the ureters of the two species studied.

It is of interest to note that in the perfusion studies it was found that the dog ureter developed much greater pressures during contraction than did the human ureter. Similarly, the enzyme studies indicate a greater quantity of cholinesterase activity in the dog ureter. It cannot at present be stated that the two phenomena are related, but the correlation bears further investigation.

DISCUSSION

In the clinical management of the obstructed and dilated ureter in the human, the problem arises as to how much alteration in the ureter is from mechanical obstructive features, how much is from the neuromuscular dysfunction, or whether both may participate in varying degrees. One of the purposes of investigation was to produce mechanically obstructed ureters in dogs. We found that such could be accomplished by the method previously described in the paper. Then, too, the contraction waves needed further analyses both in the normal and abnormal ureter. This was made possible partly by bringing together the results of cinefluorographic studies and of retrograde pyelogram data. In the moderately obstructed ureter the contraction waves were similar to those of the normal ureter. However, if the obstruction was severe the contraction wave may stop completely, as pointed out by Wislocki and O'Conor.[16] In the regenerating ureteral studies it was possible that the polyethylene tube and fibrosis added to the obstruction of the ureter. Lapides and Caffery[23] pointed out that periureteral fibrosis following intubated ureterotomy in the dog can be avoided, to considerable degree, by enclosing the operated ureter in fat and avoiding leakage of urine as much as possible. Furthermore, the periureteral fibrosis may interfere with the elastic properties of the ureter as studied by Boone and Smith.[24] On the other hand in humans Hamm and Weinberg[25] observed that there was little evidence of fibrosis or ureteral stricture at the site of ureteral linear incision if intubation was not used. Marion[26] found previously as well as others that suturing the ureter after severing it produced scarring at this site.

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[23] Lapides, Jack and Caffery, L. L. Observations on the healing of ureteral muscle relationship to intubated ureterotomy. J. Urol., 73: 47–52, 1955.

[24] Boone, A. W. and Smith, A. G. The elastic properties of the normal ureter. J. Urol., 73: 481–486, 1955.

[25] Hamm, F. C. and Weinberg, S. R. Renal and ureteral surgery without intubation. J. Urol., 73: 475–480, 1955.

[26] Marion, Henri. Étude critique et expérimentale des places transversales de l'uretère. J. d'urol. 27: 268–291, 1936.

Furthermore, the polyethylene tube itself may have played a role in the formation of fibrous tissue which in turn could produce obstruction. Cordonnier and Roane[27] observed in dogs that smooth muscle hypertrophies after prolonged splinting. Since it required about 5 weeks for the above changes to begin in dogs they recommended that the optional splinting time be 3 to 4 weeks. On the other hand Iselin[28] and many others have recommended temporary diversion of the urine flow during the healing period after ureteral surgery. He observed that if the urine flow was diverted by pyelostomy and the ureter was severed and sutured, the contraction wave did not pass the point of scarring. However, the ureter did contract on either side of the site of the scar. In addition he found that the contraction waves were more frequent proximal to the point of scarring than distal to the site of scarring; for every 2 or 3 contraction waves above the scarred ureter there was one below. From our cinefluorographic observations and regenerating ureteral studies, there appeared to be contraction waves both above and below the region of regeneration. However, these waves did not appear to be in sequence or synchronous. On the other hand the contraction waves above the regenerating, completely interrupted ureter and regenerating strip of ureter appeared to resemble those of the normal ureter.

Finally of interest is the finding by Schmidt[29] that the ureter of the aglomerular kidney of the midshipman fish can be experimentally obstructed and the ureter can be quite dilated as a result of the obstruction; yet there is no evidence of dilatation or atrophy of the secretory tubules in the kidney. This is of interest because some ureters in the human can be quite dilated and yet there is little change in the renal pelvis, calyces, and kidney function.

Improvement in the clinical management of the obstructed and dilated ureter might be achieved after structural and functional changes associated with ureteral obstruction and dilatation have received further investigation and study.

SUMMARY

Although ureteral obstruction and dilatation have created clinical problems for many years some aspects of the etiology and management of these condition remain obscure.

Various types of ureteral obstruction and regeneration were produced experimentally in dogs. The changes in ureteral enlargement and movements were subsequently studied by means of pyelography and x-ray motion pictures.

When biopsy segments of enlarged human and dog ureters were stimulated in a perfusion chamber with histamine, these contracted much more vigorously than did segments from normal ureters.

Ureteral cholinesterase was of the nonspecific type. The concentration of this enzyme was higher in the dog ureter than it was in the human ureter.

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[27] Cordonnier, J. J. and Roane, J. S.: Ureteral splinting: an experimental evaluation of prolonged ureteral splinting. Surg. Clin. North Amer., **30:** 1523–1527, 1950.

[28] Iselin, Marc: Temporary diversion of the urine by pyelostomy in repair of the ureter. Surg., Gynec. & Obst., **49:** 503–509, 1929.

[29] Schmidt, S. S.: Ureteral obstruction in the aglomerular fish. J. Urol., **73:** 226–234, 1955.

THE JOURNAL OF UROLOGY
Vol 75 No 1 January 1956
Printed in U.S.A.

EXPERIMENTAL STUDIES OF REGENERATION OF THE URETER WITHOUT INTUBATION

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In the past 5 years we have observed satisfactory repair following plastic procedures of the renal pelvis and ureter without intubation in the human subject The methods used and the followup studies of these patients have been presented elsewhere[1] Since none of the patients required secondary operations, there was no opportunity to obtain histologic evidence of repair The satisfactory postoperative roentgenograms and clinical results aroused our curiosity to obtain such evidence in the experimental animal In the dog we tried to duplicate some of the disease processes, as well as the surgical techniques used There is a tendency for fibrous tissue in the dog's ureter to undergo metaplasia and form bone in the presence of an injured urothelium This is especially true in the presence of extravasated urine Bone formation in the dog's ureter has been studied in detail by C B Huggins[2] While this phenomenon is common in the dog, it is rare in the human

It has been shown by other investigators that the ureter can regenerate all of its coats even after extensive longitudinal defects are created Table 1 is a summary of published experimental studies where extensive longitudinal defects were made in the ureter followed by the introduction of a splinting tube[3-10] To our knowledge regeneration of the ureter has not been observed in dogs in which the ureter had not been splinted Complete transection of the ureter was not made in any of these (table 1, or our) experiments, as this introduces an additional problem of interruption of blood and nerve supply that is not relevant

METHOD

Fourteen adult mongrel dogs were used The operations were done under aseptic conditions, using intravenous pentobarbitol anesthesia Penicillin and

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Read at annual meeting American Urological Association Los Angeles Calif May 16–19 1955

[1] Hamm F C and Weinberg S R Renal and ureteral surgery without intubation J Urol 73: 476–480 1955

[2] Huggins C B The formation of bone under the influence of epithelium of the urinary tract Arch Surg, 22 377–408, 1931

[3] Wiseman J L Observations on the stimulating influence of temporary rubber splinting on regeneration following ureteral resection Brit J Urol 6 11–26 1934

[4] Davis D M Strong G H and Drake W M Intubated ureterotomy Experimental work and clinical results J Urol 59 581 1948

[5] Kimbrough J C Furst J N Worgan D K and Denslow J C Intubated ureterotomy Report of animal experimentation and clinical cases J Urol 64: 74–84, 1950

[6] Trautner K and Raaschow F Histological examination of regeneration of ureter in dogs after intubated ureterotomy J Urol 71: 274–286, 1954

[7] Weaver R G and Henderson J H Ureteral regeneration experimental and clinical J Urol 72 350–357 1954

[8] Lapides J and Caffrey E L Observations on healing of ureteral muscle Relationship to intubated ureterotomy J Urol 73 47–52, 1955

[9] Bovarsky S and Duque O Ureteral regeneration in dogs An experimental study bearing on the Davis intubated ureterotomy J Urol, 73 53–61 1955

[10] Vest S A Conservative surgery in certain benign tumors of the ureter J Urol, 53: 97 121 1945

TABLE 1

Name of Investigator	Linear Ureterotomy	Longitudinal Defects in Ureter	Type of Splint	Regeneration	Sequelae
Wiseman, 1934	0	1	No. 4–5F catheter	Yes	Good healing of defect; kidney showed only minimal inflammation.
Davis, 1948	0	6	Large size ureteral splint	Yes	Kidney removed in all cases.
Kimbrough, 1950	4	0	No. 6F catheter tube	Yes	Hydronephrosis and calculi in three of the 4 dogs.
Trautner, 1954	0	9	Polyethylene tube	Yes	Varying degrees of hydronephrosis in seven of the 9 cases. Two cases with good renal structure after operation.
Weaver, 1954	0	16	No. 8F soft rubber catheter	Yes	Scar tissue and inflammatory reaction due to urinary extravasation. No observations of renal function.
Lapides, 1955	0	28	No. 18 gauge polyethylene tube	Yes	In 20 cases kidneys removed, periureteral adhesions and hypertrophy about splint; 1 kidney destroyed; 5 kidneys, varying degrees of pyelonephritis; 2 normal caliber ureters.
Boyarsky, 1955	0	11	Partially flexible polyethylene tube	Yes	1 dog had kidneys removed; 2 kidneys destroyed; 2 kidneys with normal morphology; ureters were enlarged, thickened with fibrous reaction.

streptomycin were administered to all dogs for 1 week postoperatively. The kidneys were inspected, palpated, and found to be normal in all the dogs that were used.

In 3 dogs a linear ureterotomy, consisting of an incision through all the coats of the midureter for a distance varying from 2.5 to 3.0 cm., was done. The incision in the ureter was not sutured, nor were any splinting catheters or nephrostomy tubes used. The urine from the incised ureter was drained to the exterior by means of a latex rubber (Penrose) drain. The drains were bivalved and sutured to the surrounding skin in order to prevent the animal from chewing them out. As an additional precaution, the wound was then covered with an abdominal binder. The Penrose drain was left in place until urinary drainage had ceased.

Two points of technique need to be emphasized: 1) The ureter should not be disturbed from its bed or stretched any more than absolutely necessary during the operative process. 2) If its position has been disturbed, it should be carefully replaced to prevent angulation.

Figure 1 illustrates the result of excessive mobilization of the ureter outside

FIG. 1

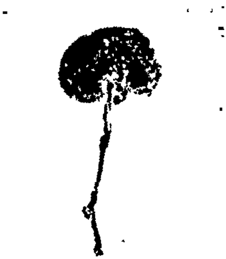

FIG. 2

FIG. 1. Excretory urogram 21 days after linear incision of right ureter. Note angulation at point of incision.
FIG. 2. Dog No. 474. Kidney and ureter removed 21 days after linear ureterotomy.

its bed. Severe stretching and distortion may produce redundancy and obstruction.

RESULTS

No deaths occurred. The wounds in all 3 animals that had linear ureterotomy healed promptly. The longest period of urinary drainage was 7 days. The dogs appeared healthy and normal on the first postoperative day. In two of the 3 animals, the ureter healed with adequate lumen; no evidence of hydroureter or hydronephrosis (fig. 2) and no gross evidence of infection were found. Figure 3 depicts a section through the incised area of the ureter of dog No. 474. If not for the marking sutures, we would be unable to differentiate it from the unoperated portion. Only a minimal infiltration of round cells was found in the parenchyma of the companion kidney (fig. 3, *C*). In view of Dempster's[11] findings that over 50 per cent of mongrel dogs have histologic evidence of chronic nephritis, characterized by infiltration of round cells; this observation is probably of no clinical importance. The result obtained in the third animal, previously shown (fig. 1), indicates good renal function with minimal delay in excretion of the visualizing dye.

In the remaining 11 dogs, an extensive longitudinal defect produced by the removal of one-half to one-third of the ureter was made (fig. 4) and regeneration observed. The site of defect was marked by 5-0 silk sutures through the serosa; they measured from 2.5 to 3.0 cm. in length. The defects were not sutured, nor were any splinting tubes used. Urinary drainage was provided by rubber tissue

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[11] Dempster, W. J. and Joekes, A. M. Functional studies of the kidney autotransplanted to the neck of dogs. Acta med. Scandinav., 147: 99–118, 1953.

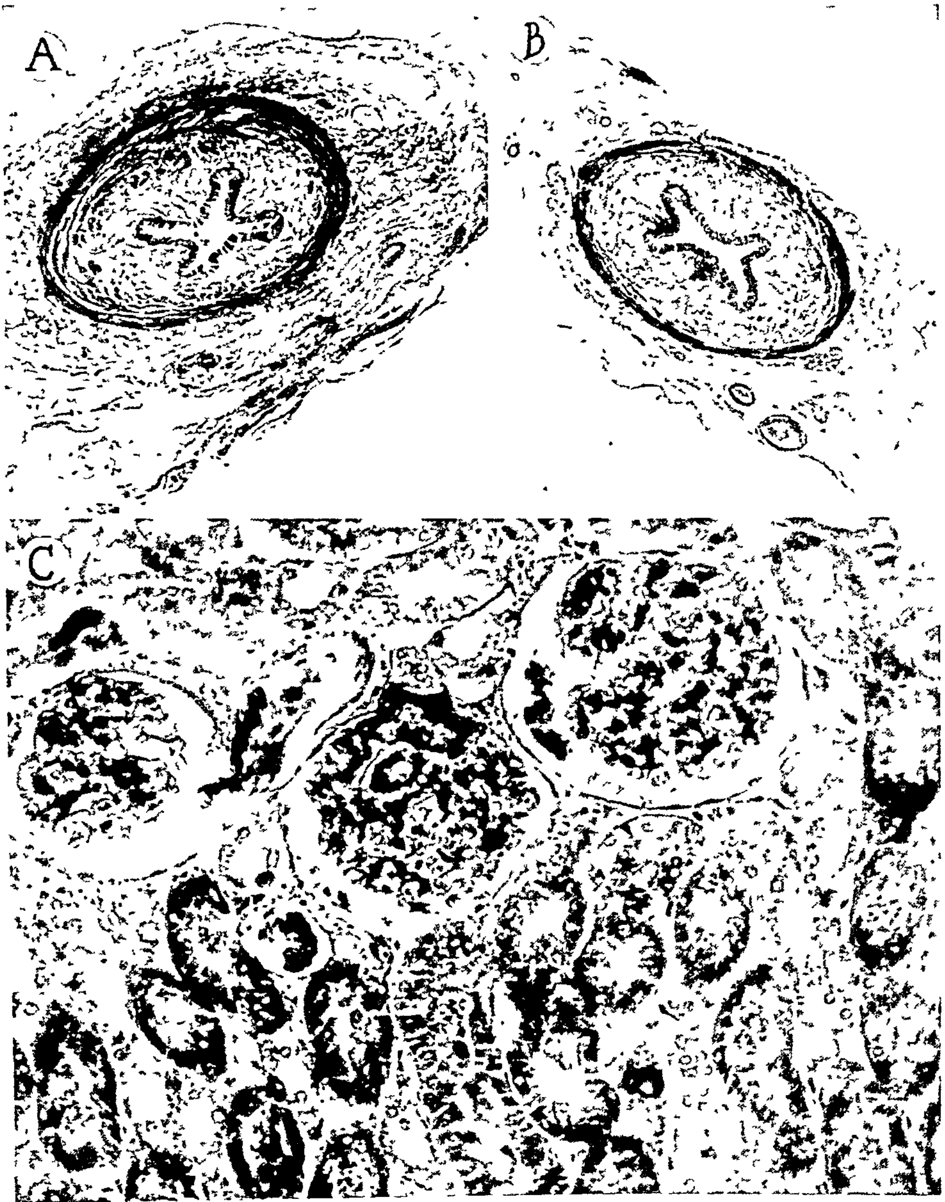

FIG. 3. Dog No. 474. Linear ureterotomy 21 days postoperatively. *A*, section through unoperated area. *B*, section through incised area. *C*, histologic appearance of kidney 21 days after linear incision.

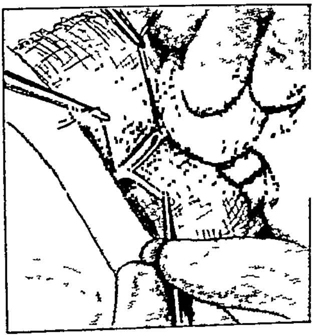

FIG. 4. Semidiagrammatic drawing showing excision of defect in ureter. Note marking, nonabsorbable sutures to delineate site of defect.

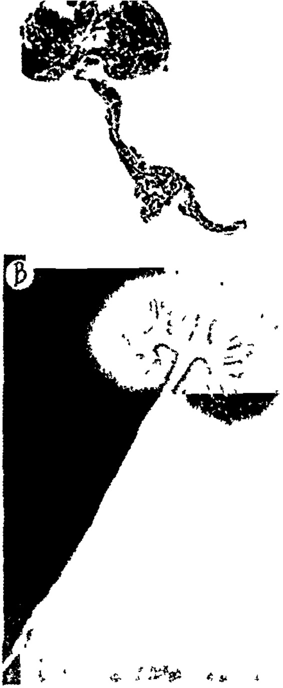

Fig. 5 Dog No. 583. Partial ureterectomy 57 days postoperatively Complete ureteral continuity and normal pyelogram.

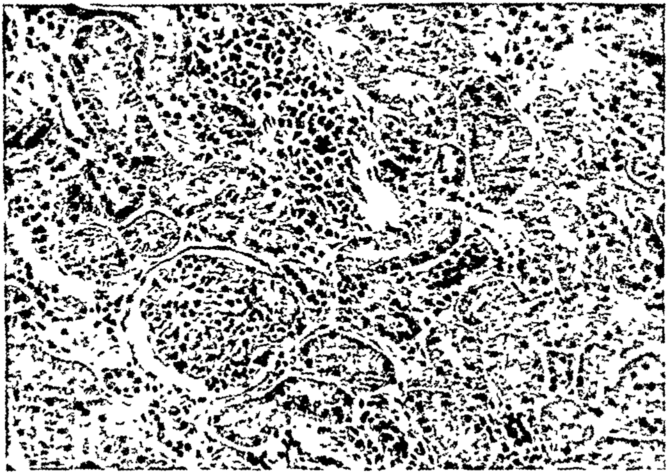

Fig. 6 Dog No. 583 Histologic appearance of kidney 57 days after partial ureterectomy

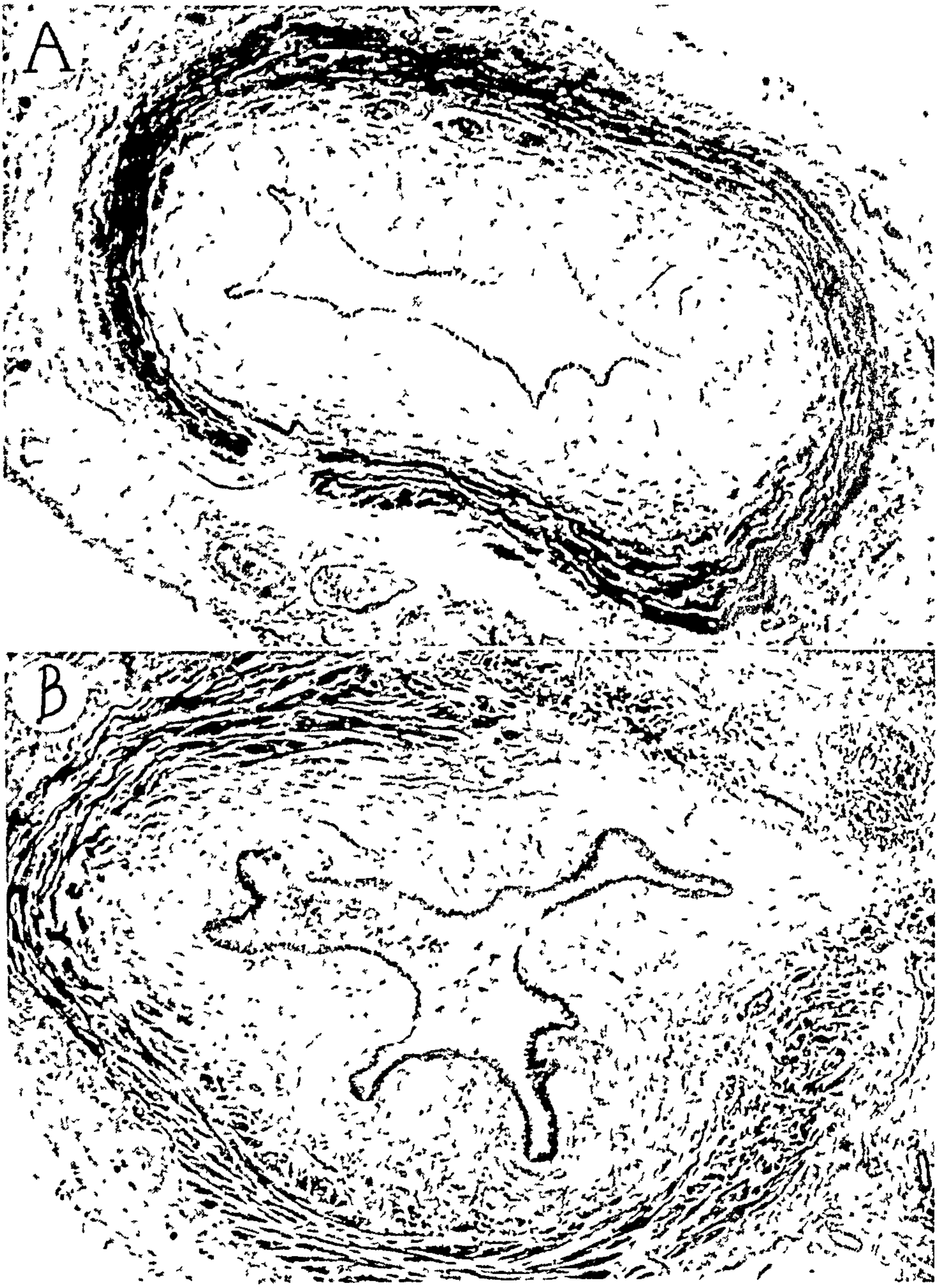

Fig 7 Dog. No 583. *A*, partial ureterectomy 57 days postoperatively, section through unoperated area *B*, section through regenerated area showing defect in muscle filled with fibrous tissue (right).

passed down to the site of the defect by a technique similar to that previously described. The animals were then allowed varying intervals of convalescence.

RESULTS

Of the 11 dogs, a good result was obtained in seven. All the dogs survived the operative procedure. Except for one dog that died suddenly on the fourteenth

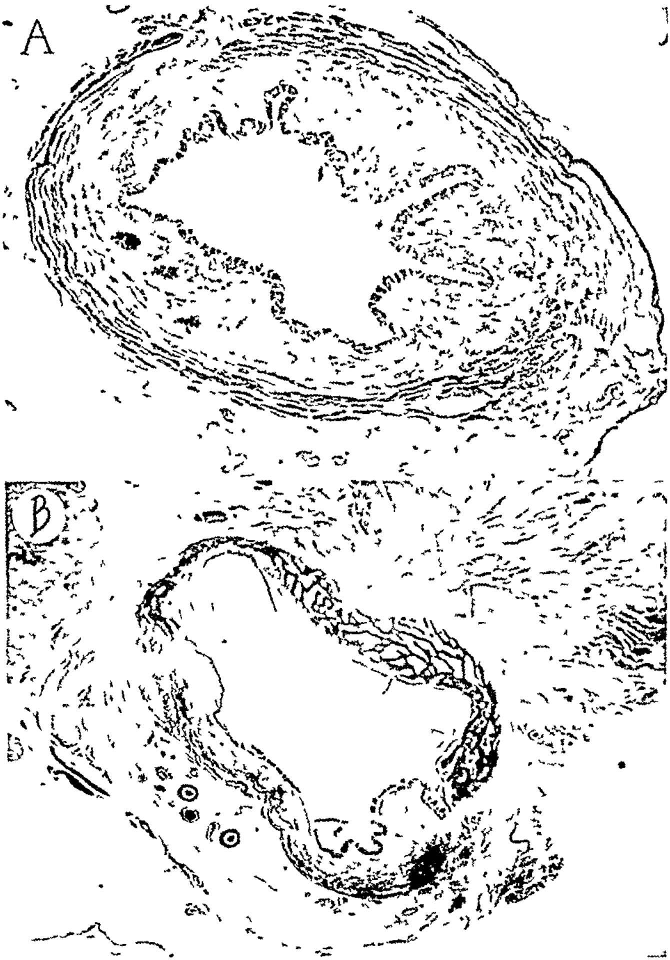

FIG 8 Dog No 626 Partial ureterectomy 36 days postoperatively *A*, section through unoperated area *B*, section through area of regeneration, despite ossification in wall there is an adequate lumen

postoperative day, all the animals had elective secondary nephroureterectomies after varying intervals of convalescence ranging from 21 to 150 days The one dog that died had showed a small amount of serofibrinous exudate in the regions of the ureteral wound, but no other marked pathologic change in any of the organs In this animal, healing had proceeded satisfactorily, with no evidence of ureteral obstruction or renal infection. We believe that some extraneous process may have caused this death. After the ureters and kidneys on the operated side were completely removed, they were first filled with radiopaque substance to obtain pyeloureterograms (fig. 5). They were then sectioned for histologic studies.

We were able to demonstrate complete regeneration of the mucosa of the ureter in all the dogs. As stated in seven of the 12 dogs, the ureter healed with adequate lumen. The kidneys were examined and no important gross or microscopic abnormalities were noted (fig. 6). An adequate lumen completely lined by epithelium was noted as early as fourteen days postoperatively. Replacement of the muscularis of the ureter takes place after the defect has been filled with fibrous tissue (fig. 7). The muscle is thin at first, but in animals where the ureter was allowed a longer period of regeneration, normal thickness can be seen. In three of the ureters, muscle was partly replaced by bone in the area of the defect. But in spite of this, an adequate ureteral lumen and normal renal morphology were found (fig. 8).

In the remaining 4 dogs stricture formation occurred at the site of defect, resulting in varying degrees of hydronephrosis. In three instances, animals extracted their drains the day after operation. This was followed by clinical evidence of urinary extravasation. They took nourishment poorly, were listless and febrile. After a few days, they recovered. The dogs that retained their drains had no such reaction; they were able to exercise, take nourishment normally, and had no postoperative elevation of temperature. In the remaining dog, there is no apparent reason for the poor result and it must therefore be considered a failure.

DISCUSSION

After microscopic study we were unable to differentiate between regenerated muscle and muscle obtained from an unoperated site. It has been suggested by Dr. A. deVeer,[12] who reviewed our sections, that it is possible for the strip of ureter remaining after a defect is created to reform itself into a small tube and as urine is forced through it, increased lumen may result. This phenomenon is observed in regeneration of the bladder following subtotal cystectomy. Hinman[13] has emphasized the importance of this hydrodynamic effect upon healing of the ureter. In his laboratory he was able to produce a dilated ureteral lumen by suturing a longitudinally incised ureter to the retroperitoneum, and letting it heal of its own accord. As Lapides[8] has suggested, a differential stain would be helpful in distinguishing between new or hypertrophied smooth muscle. Prolonged intubation often produces a foreign body reaction. Cordonnier and Roane[14] have presented histologic evidence that the prolonged use of a splint in a dog's ureter results in increased vascularity and lymphocytic infiltration. After 3 weeks of intubation there is excessive muscular hypertrophy in the walls. The presence of a catheter also favors contamination of the urine with urea-splitting organisms Fibrosis is also favored by infection and the presence of extravasated urine about the adventitia of the ureter.

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[12] deVeer, A.: Personal communication.

[13] Hinman, F. Jr.: Plastic operations on the ureter and renal pelvis. Personal communication.

[14] Cordonnier, J. J. and Roane, J. S.: Ureteral splinting: An experimental evaluation of prolonged ureteral splinting. Surg. Clin. North Amer., 30: 1523-1527, 1950.

CONCLUSIONS

Regeneration of the ureter after linear incision or partial ureterectomy can occur without intubation or urinary diversion from the kidney.

Adequate urinary drainage (by Penrose drain) is essential, in order to prevent stricture at the operative site in the experimental animal.

Renal function is maintained in a favorable state after ureteral surgery when splinting tubes are not used.

The Journal of Urology
Vol. 75, No 1, January 1956
Printed in U S A

USE OF A LOCK SPLINT IN INTUBATED URETEROTOMY

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The value of a ureteral splinting catheter in the repair of a defect in the wall of the ureter is well established. The basic principles have been presented by Davis, but numerous modifications facilitating the procedure have been made since his original report.

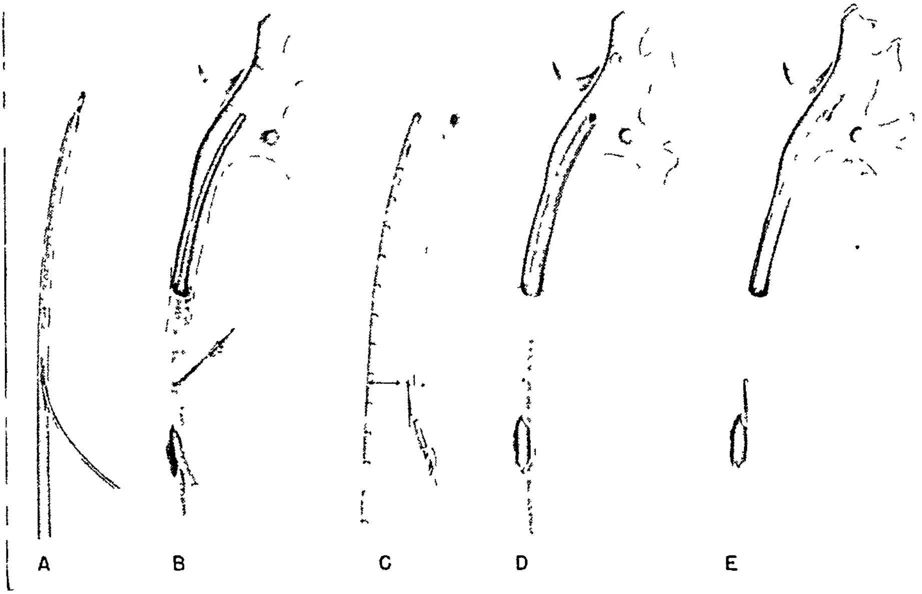

Fig. 1. *A*, diagram of assembled splint. *B*, ureteral wall is pierced for insertion of locking catheter. *C*, opening is drilled at an acute angle to long axis of splinting catheter. *D*, splinting catheter in ureter. *E*, locking splint in situ.

The following modification deals with plastic splinting material, an improvement in keeping the splint in place and ease of removing the splint. Though a splint can be placed in the ureter with a distal end left in the bladder for short periods,[1] it is generally agreed that where longer periods of splinting are planned, the kidney pelvis should have additional drainage. Without other drainage the hydrostatic bladder pressures would be reflected to the renal pelvis. In cases where the lesion to be repaired in the ureter is below the renal area, it has been customary to do an additional operation with another incision to provide pyelostomy or nephrostomy drainage or compromise splinting by the use of a T tube. With this modification we have been able to provide for drainage of the renal pelvis during the splinting period by inserting the splints through the

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Read at annual meeting, Southeastern Section of American Urological Association, New Orleans, La. March 20-24, 1955.

[1] Senger, F. L. and Zorgniotti, A W : J. Urol , 69: 372, 1953.

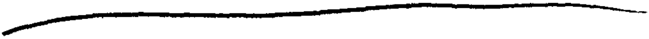
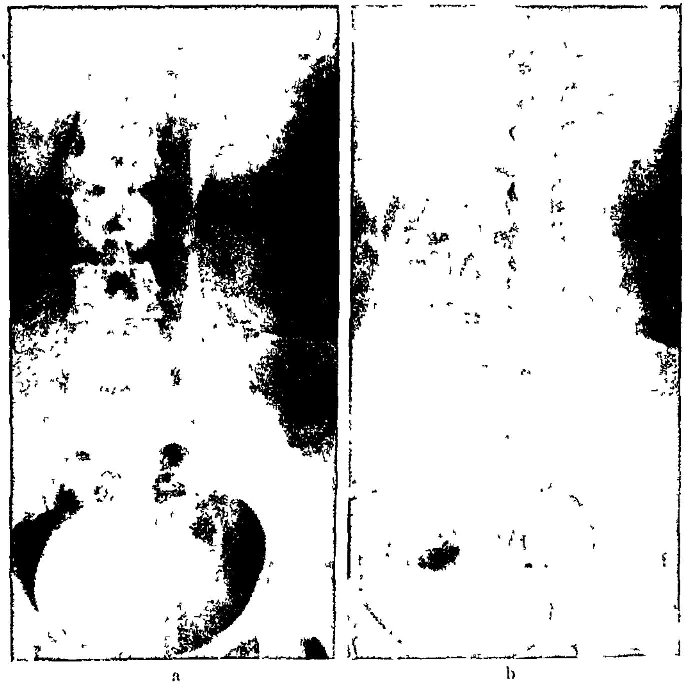


FIG. 2. Prepared white polyvinyl catheter splint size 10F Its lumen will accommodate a size 7F polyethylene locking catheter.

operative incision when making a repair of the lower ureter, obviating the need for a nephrostomy or pyelostomy.

The development of the newer splinting materials has resulted in a catheter with a thinner wall and a larger lumen. This makes it possible to insert a fairly large polyethylene catheter into the lumen of the splinting catheter, which locks the splint in place and drains the renal pelvis. Note that the location of the small hole to be drilled through the wall of the splinting catheter is determined by measuring with a graduated ureteral catheter (fig. 1, *B*).



a b

FIG 3 (Left), preoperative excretory urogram of patient with intermittent uretero-vaginal fistula following gynecological surgery. (Right), postoperative result after dissection of fistula and scar Defect in wall of ureter 3 cm in length was treated by lock splint technique

Recently white polyvinyl has been used to make the specially prepared ureteral splint (fig. 2). This material appears to possess most desirable characteristics for this splint. It is flexible and yet has enough rigidity so that the catheter can be made with a thin wall and relatively large lumen. White polyvinyl is not yet as effective as polyethylene in preventing the deposition of crystals on the splint. Boyd has used white polyvinyl in his ureteral splint and states that thus far he has found no objection to it as a splinting material.[2]

When the splinting catheter is to be removed the locking splint is removed first. This frees the splinting catheter, which is then removed through the cystoscope by picking up the coiled end which lies free in the bladder.

My experience thus far with this type of splinting has been so satisfactory (fig. 3) that I will continue to use it in patients where the introduction of a nephrostomy or pyelostomy tube would require a second surgical procedure.[3]

I wish to express appreciation for the co-operation of Mr. Frederick J. Wallace of American Cystoscope Makers, Inc., New York, N. Y.

Appreciation is also expressed to the School of Medical Illustration, Medical College of Georgia.

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[2] Boyd, M. L. and Holsenbeck, G. H.: J. Urol., 73: 674, 1955.

[3] Rinker, J. R. and Gillespie, S. D.: Trans. Southeastern Section, Am. Urol. Assn., 1954, p. 145.

The Journal of Urology
Vol 75, No 1, January 1956
Printed in U S A

AN IMPROVED BASKET BOUGIE FOR EXTRACTION OF URETERAL CALCULI

HENRY S BROWNE

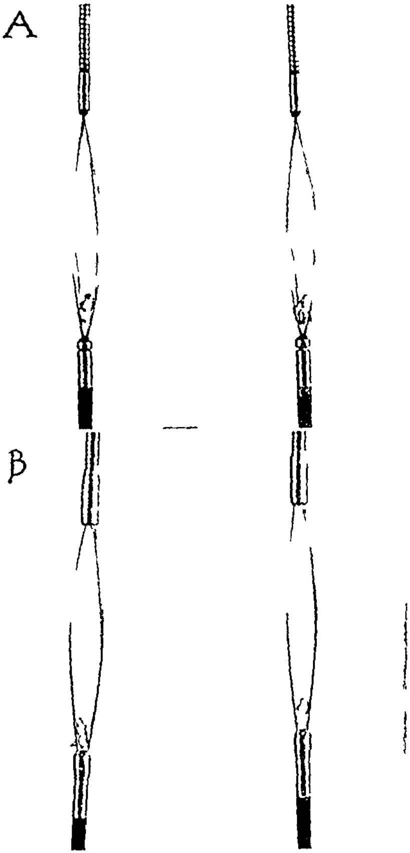

Fig 1 *A*, Johnson basket with stone engaged Note that wires come together in a point so stone can slip out easily *B*, modified basket with stone engaged and resting firmly against base from which it cannot slip out easily

The Johnson basket bougie marked a step forward in the treatment of ureteral stones, in that a small stone in the lower ureter could be caught in the basket and often extracted Those of us who have used this instrument have often been

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Read at annual meeting, Oklahoma Urological Society, Tulsa, Okla May 7, 1955 aggravated by having the stone caught, drawn down and almost into the bladder, only to slip out at the last moment and remain in the ureter. This is because the wires of the basket are inserted into the center of the bougie thereby coming to a point against which the stone cannot rest and thus allowing it to slip out. This also makes the bougie fragile so that it loses its shape easily. Recently I have had C. R. Bard, Inc. make a modified model in which the wires are inserted into the outer edge of the bougie, thereby leaving a pocket at the base against which the stone can rest while being drawn down, thus preventing it from slipping out of the basket easily. In addition, the instrument (fig. 1) is much stronger than the original bougie, as the wires, being inserted in the outer edge, act as a support for one another, so that the basket does not get out of shape so readily. I have used this instrument in five successive cases in which the stone was engaged and in no case did the stone slip out. There also did not seem to be nearly so much pull necessary in extraction as with the Johnson basket bougie.

Medical Arts Bldg., Tulsa, Okla.

The Journal of Urology
Vol. 75, No. 1, January 1956
Printed in U.S.A.

ECTOPIC URETER OPENING INTO A SEMINAL VESICLE

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Anomalies of the urinary tract comprise approximately ten per cent of all congenital malformations (Campbell). One of the rare types of the genitourinary tract anomalies is an ectopic ureter opening into a seminal vesicle. This unusual anomaly has been previously reported and diagnosed clinically on only 9 occasions (table 1). In addition, 32 cases were found at autopsy.

The embryological explanation has been reviewed by others and understood by us in the following manner. Between the fifth and sixth weeks of fetal life, the cloaca is divided by a frontal fold into a dorsal rectal and ventral urogenital segment. The renal collecting system is formed by a posterior budding from the wolffian duct which empties into the urogenital segment. The wolffian duct and ureter are ultimately completely separated from each other as the former forms the posterior urethra, vas deferens, epididymis, and seminal vesicles, the orifice of the latter is carried upward into the lateral angle of the trigone. Thus failure of complete separation of these two structures results in connection of the systems which is manifested by various types of ectopic ureteral openings into structures of the seminal tract.

Our case is the tenth reported one of an ectopic ureter opening into a seminal vesicle which was diagnosed clinically. We believe, because of its rarity and the unusual method of diagnosis, that it worthy of a report.

CASE REPORT

A 42-year old white man was admitted to the Sinai Hospital of Baltimore, February 8, 1954, with the chief complaints of dribbling at the end of urination, voiding with a spray-like stream, and diminution in the strength of his stream. These symptoms had been present for over three years. The patient had three cystoscopic examinations prior to this admission, the diagnosis was agenesis of the right kidney and a cyst of the seminal vesicle on the right. The patient had been to another clinic because of sterility. Otherwise, his past history was noncontributory.

On physical examination the right testicle was smaller than the left, rectal examination revealed the prostate to be normal. A fullness was palpated in the region of the right seminal vesicle.

The patient had a cystoscopic examination on February 9, 1954. A lobulated globular mass, situated in the region of the right side of the trigone and protruding upon the right posterolateral aspect of the bladder neck, was found. The left ureteral orifice appeared normal, the right ureteral orifice was not visualized. Indigo carmine, which had been injected intravenously, appeared on the left side in 6 minutes and in good concentration. There was no evidence of dye coming from the region of the right side of the bladder or from the posterior urethra.

Read at annual meeting, Mid Atlantic Section of American Urological Association, Atlantic City, N. J., April 14–16, 1955.

* Present address: Denver, Colo.

TABLE 1. *Cases of ectopic ureter opening into seminal vesicle which were diagnosed clinically*

Author	Age	Side	Fertility	Presenting Complaint	Method of Diagnosis	Treatment	Cond. of Kidney
Day, R. F., 1924	21	left	?	Severe left lumbar pain following fall (pyuria)	Catheterization of opening in posterior urethra. Pyelograms	Surgical removal of kidney and ureter.	Hydronephrosis and pyonephrosis
Culver, Harry, 1937	50	left	?	Pyuria found on insurance exam.	I.V.P. revealed ectopic opening	None required	Ectopic double kidney
Hamer, H. G., Mertz, N. O. and Wishard, W. N., Jr., 1937	25	right	?	Painful urination	Cystic mass in bladder punctured & catheter passed	Endoscopic drainage	Not visualized by x-ray
Riba, L. W., Schmidlapp, C. J., Bosworth, N. L., 1946	19	left		Severe left flank pain following injury (pyuria)	Ejaculatory ducts catheterized.	Surgical removal of kid., uret. & sem. ves.	Hydronephrotic double kidney (upper)
Engel, W. J., 1948	21	left	Sterile	Unable to conceive	Opening in post. urethra catheterized & x-ray studies carried out.	None. Advised surgery	Hypoplastic
Hamilton, G. R. and Peyton, A. B., 1950	20	left		Rt. upper abdominal pain & hematuria followed blow to right abdomen.	Cystic mass in bladder punctured with electrode. Catheter passed for pyelo. Vasoseminal vesiculogram	Surgical removal of kidney, ureter & sem. ves.	Hypoplastic
Meisel, H. J., 1952	28	left	Fertile	Squeezing sensation in rectum	Vasoseminal vesiculography	Surgical removal of kid., ureter & sem. ves.	Hypoplastic
Pasquier, C. M. and Womack, R. N., 1953	26	right	?	Enuresis	Cystic mass in blad. punctured with electrode. Cath. passed for pyelo. Vasoseminal vesiculogram	Surgical removal of kid., uret. & sem. ves.	Hypoplastic
O'Malley, J. F. and Bumgarner, J. E., 1955	27	left	Fertile	Hematuria hemaspermia	Excretory urography	Vasectomy. Antibiotics	Hypoplastic
Goldstein, A. E. and Heller, E., 1955	42	right	Sterile	Difficulty passing urine. Split stream	Vasoseminal vesiculography	Surgical removal of kid., uret. & sem. ves.	Hypoplastic

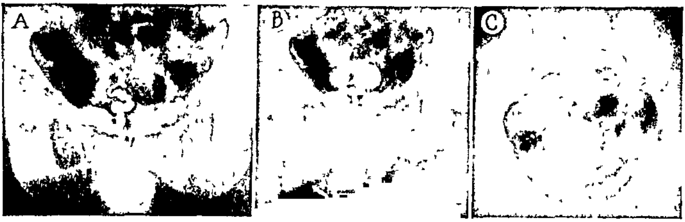

FIG. 1. *A*, seminal vesiculogram made after injecting 1.5 cc 30 per cent urokon on each side. Note normal seminal vesicle on left. *Ampulla of right vas deferens is dilated. Right* seminal vesicle is abnormal and much enlarged. Right ejaculatory duct is obstructed. *B*, film taken after 10 cc 70 per cent urokon had been injected on right side. Note tortuous, dilated, globular structure leading from dilated seminal vesicle, probably right ureter. *C*, 150-minute retention film. Note that dye extends into dilated ureter to level of right sacroiliac joint.

It was suspected that the seat of the process was in the region of the right seminal vesicle, and therefore a bilateral vasoseminal vesiculogram was made by means of exposing the vas on each side in the upper part of the scrotum. A hypodermic needle was inserted into the lumen of each vas and 70 per cent urokon sodium injected.

The first seminal vesiculogram was taken after 1.5 cc of dye was injected on each side. It revealed a normal left seminal vesicle and a dilated ampulla of the vas along with a deformed vesicle on the right (fig. 1, *A*). The second vesiculogram was taken after 10 cc of dye was injected on the right. The contrast medium entered a dilated, tortuous, lobulated channel in the region of the right seminal vesicle (fig. 1, *B*). A 150-minute retention film revealed the progression of dye into a dilated, curved channel which extended to the level of the right sacroiliac joint (fig. 1, *C*). The 24-hour retention film revealed retained dye in the previously described area along with further progression of dye up to the level of the fifth lumbar vertebra on the right which appeared to be a dilated right ureter. An excretory urogram taken at the same time showed a normal left upper urinary tract with a filling defect in the right side of the bladder (fig. 2). These findings, together with the cystoscopic picture, were indicative of an ectopic ureteral opening into the right seminal vesicle with a hypoplastic right kidney and right hydroureter.

On February 16, 1954, an exploratory operation was carried out. The lower portion of the right ureter was exposed through a right Gibson incision. It was found to be dilated below the region of the fourth lumbar vertebra and normal above that point. The ureter was dissected down to the posterior wall of the bladder where a cystic, lobulated, globular mass was found. This mass was posterior to the bladder and was a continuation of the ureter. A cystotomy was performed during the dissection; it was noted that the right ureter did not communicate with the bladder. Further dissection exposed a large right seminal vesicle which was not distorted in appearance. The ureter opened into the ampulla of the seminal vesicle. The right seminal vesicle was removed with the pelvic portion of the vas deferens. The ureter was freed from its attachments to the seminal vesicle and bladder wall and was brought out through the incision. Since the

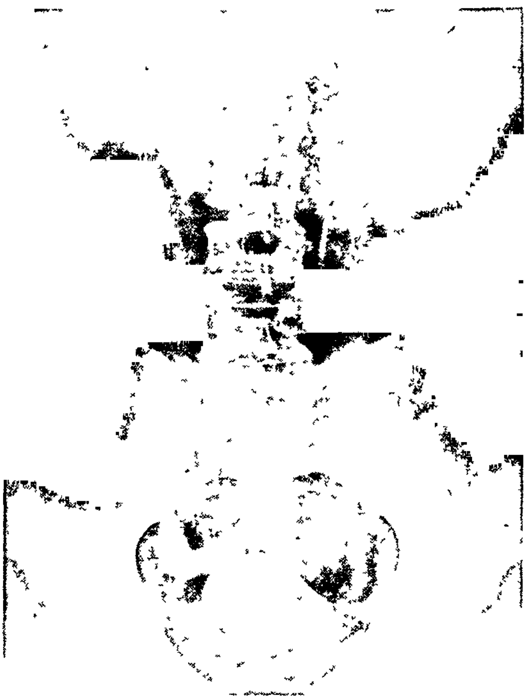

FIG. 2. Twenty-four-hour retention film coupled with an 8-minute excretory urogram. Note normal left kidney, filling defect on right side of bladder, dye in right seminal vesicle and lower end of right ureter extending to level of lumbosacral joint on right side.

general condition of the patient was not too satisfactory, a second operation was decided upon for removal of the right kidney. The specimen was allowed to remain intact on the abdomen.

One week later on February 23, 1954, a hypoplastic right kidney, in normal position, was removed, with the attached dilated ureter and seminal vesicle through a right flank incision (fig. 3, *A* and *B*). The patient had a bothersome postoperative course because of various allergic manifestations. At the time of discharge from the hospital, his urinary complaints had been alleviated.

Cases of an ectopic ureter opening into a seminal vesicle found at autopsy were reviewed by McKirdie and Polkey also by others.

Hamer, Mertz, and Wishard, Jr., reporting later, added two more cases found at autopsy and one discovered clinically. Riba, Schmidlapp, and Bosworth in 1946 reviewed the literature on this anomaly and included ectopic ureteral openings in other parts of the seminal tract. They found 36 cases in all; of these, thirty-two were noted at autopsy and four clinically. In 10 cases the ureter drained into the vas deferens or ejaculatory duct. It is interesting to note that of the 32 cases reported at autopsy the condition occurred 21 times on the left and 10 times on the right side; the ectopic ureter was single in 26 cases and reduplicated in 6 cases. The corresponding kidney was rudimentary in 14 cases, absent in ten, fibrosed in two, normal in one, and was a double one in three.

Day, in 1924, diagnosed this entity by means of catheterization of an opening seen in the posterior urethra. In 1937, Culver found the ectopic opening on an excretory urogram which had been done as part of a study for pyuria. Hamer,

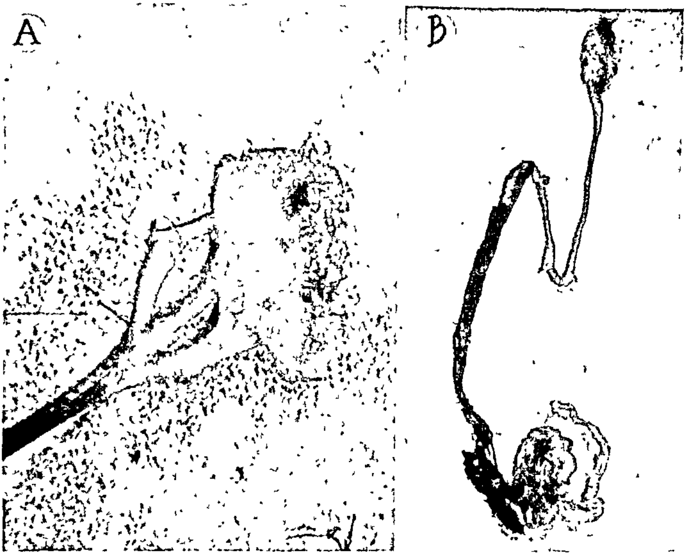

FIG. 3. *A*, gross spe [illegible] and its three extrarenal divisions of
ureter which are probal [illegible] 3.5 by 2 cm. *B*, entire gross specimen
of hypoplastic kidney, [illegible] dilated seminal vesicle and section of
vas deferens.

Mertz, and Wishard, Jr., in 1937, catheterized an opening in a bladder "cyst" which had been created by cystoscopic scissors and through this performed the diagnostic pyelogram. As the persistent pyuria following nephrectomy cleared after prolonged stripping of the right seminal vesicle, they assumed that the hydroureter emptied into the right vesicle.

Riba, Schmidlapp, and Bosworth, after two exploratory operations with excision of the upper pole of the double kidney, diagnosed the primary process by means of catheterizing the ejaculatory ducts and taking vesiculograms. Engel, in 1948, diagnosed this entity by means of catheterizing an opening found in the posterior urethra and performing radiographic studies subsequently. Hamilton and Peyton, in 1950, punctured a "cystic mass" in the bladder with an electrode and passed a ureteral catheter through the opening; subsequent pyelograms revealed the pathologic entity. In this particular case, vasoseminal vesiculography was done as a diagnostic check.

In 1952, Meisel diagnosed this condition by means of vasoseminal vesiculography. Pasquier and Womack, in 1953, diagnosed the condition in exactly the same manner as Hamilton and Peyton. They confirmed their diagnosis by means of catheterizing the vas deferens and performing seminal vesiculograms. In February 1955 O'Malley and Bumgarner reported an additional case, diagnosed by excretory urography. In their case the dye was seen to have filled the left seminal vesicle after it left the ureter.

DISCUSSION

In reviewing the case presentations of the subject under discussion, certain diagnostic features stand out. In 6 cases a globular mass was found in the bladder on cystoscopy. The corresponding ureteral orifice was absent in all but O'Malley and Bumgarner's case; a nonfunctioning kidney was present in six. On rectal examination a fullness or mass was found on the affected side five times (rectal examination was not mentioned in 5 cases).

The corresponding kidney was pathologic in all cases but O'Malley's. His case demonstrated hypoplasia without pathological change. The pathologic entity includes hypoplasia six times, hydronephrosis two, and double kidney in two.

Although sterility was not constant enough to be a diagnostic factor, it was present in 2 cases. Pyuria was found in 6 patients.

It is apparent that the diagnostic picture is not constant in all cases. Nonvisualization of the kidney in the presence of a globular mass in the bladder, occupying one side of the trigone, is an important observation. The absence of the corresponding ureteral orifice and a fullness or mass in the region of the seminal vesicle of the involved side should cause one to suspect an ectopic ureter opening into that structure. If the entity is not thought of, the diagnosis might be missed.

SUMMARY

A brief review of ectopic ureter opening into a seminal vesicle is presented.

A review of those cases which were diagnosed clinically is included.

The diagnosis can invariably be made by seminal vesiculography.

The diagnosis of a congenital absent kidney should be followed by vasoseminal vesiculograms in search of an ectopic ureter opening into the seminal structures.

Six of the ten reported cases showed renal hypoplasia on the same side.

The tenth case clinically diagnosed is presented in detail.

Addendum: Since the preparation of our paper, one more case has been reported by Doctors Gartman and Cline (U. S. Armed Forces Med. J., 5: 1668–1671, 1954).

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THE JOURNAL OF UROLOGY
Vol. 75, No. 1, January 1956
Printed in U.S.A.

TRANSURETHRAL INTRAMURAL INJECTION OF HYDROCORTONE HYALURONIDASE FOR INTERSTITIAL CYSTITIS (HUNNER'S ULCERS)

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The 9 patients presented here are women. We are all familiar with the symptoms and signs of interstitial cystitis. Anatomically the peritoneum is attached to the distensible portion of the bladder. When interstitial cystitis is present, always in the distensible portion of the bladder, the perivesical inflammatory reaction causes an inflammation of the adjacent peritoneum with the development of abdominal pain. The treatment proposed here is directed toward this lesion.

With the patient under general anesthesia, the procedure consists of overdistension of the bladder, under vision, to locate the lesions. Injections are made with the bladder only slightly distended.

Technique of transurethral intramural injection: Multiple injections are made using 2 cc per injection beginning first at the periphery of the interstitial area causing an induced bullous edema. The injection is first made into the submucosa and then deeper into the bladder musculature. The center of the interstitial area where the fibrosis is the most dense is reserved for the final injection. In an old, long-standing scarred lesion it is impossible to inject into the center of the scar and one has to be satisfied by injections into the periphery as close as possible to the center of the lesion.

The injection is made with a long flexible needle having interchangeable straight or curved tips. This needle is used through a carrier and adapter accommodating the 68A foroblique telescope fitted to the short beaked sheath of the Stern McCarthy resectoscope (fig. 1).

The optimum dose was 250 mg. hydrocortone and 1500 turbidity units of hyaluronidase in a total volume of 30 cc normal saline. Larger amounts of hydrocortone hyaluronidase were used in some patients (a maximum of 2500 mg. hydrocortone and 3000 turbidity units of hyaluronidase). There is no advantage in the larger dose.

Total eosinophile counts done on these patients showed a decrease to an absence in number of eosinophiles following injection by comparison to the control period, proving that hydrocortone was absorbed. Nevertheless, no impairment of renal function was noted.

We should consider here the action and reaction of hydrocortone and hyaluronidase. These compounds are antagonistic but the time sequence of their absorption makes it possible for them to be clinically effective. The maximum hyaluronidase effects lasts for 12 hours although some slight activity persists for a total of 48 hours. Its purpose is to spread the hydrocortone diffusely into the fibrotic

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Read at annual meeting, American Urological Association, Los Angeles, Calif. May 16-19, 1955.

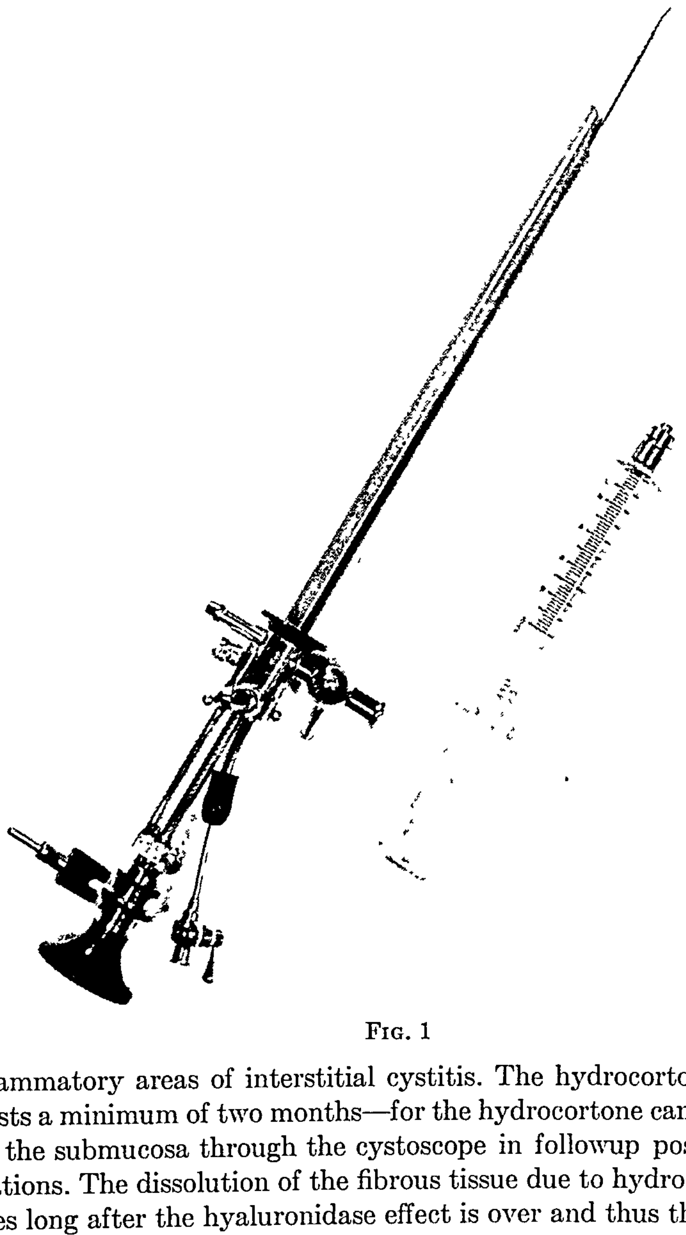

FIG. 1

and inflammatory areas of interstitial cystitis. The hydrocortone, on the other hand, lasts a minimum of two months—for the hydrocortone can be seen as white areas in the submucosa through the cystoscope in followup postoperative office examinations. The dissolution of the fibrous tissue due to hydrocortone therefore continues long after the hyaluronidase effect is over and thus these theoretically antagonistic drugs actually complement each other when used with an excess of hyaluronidase for this purpose.

The immediate postoperative results are a frequent desire to void and abdominal pain lasting about 12 hours followed by a sudden disappearance of pain and pollakiuria. The beneficial results including the relief of pain last approxiately 2 to 9 months or longer. Subsequent examinations under anesthesia with overdistension reveal that the sites of the original lesions are healed, do not split on stretching, do not bleed and are normally distensible. New interstitial areas do develop in different portions of the bladder from those injected and always in the distensible portion, but the patient should be given the benefit of subsequent transurethral injection treatment. The injection of hydrocortone hyaluronidase into such a site is not contraindicated.

In conclusion we wish to emphasize that the simultaneous transurethral intramural administration of hydrocortone and hyaluronidase for the management of interstititial cystitis is not a cure but a symptomatic relief for a distressing disease.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 1, January 1956
Printed in U.S.A.

PRESENT UROLOGIC STATUS OF THE WORLD WAR II PARAPLEGIC: TEN-YEAR FOLLOWUP

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In view of the paucity in the literature of long term followups of any sizeable group of paraplegic patients, we felt it might be worthwhile to evaluate the present urologic status of the 170 cord injury patients who were the subject of a similar review by Hutch and Bunts in 1949. We found many of these patients, now averaging 9 years since the onset of paralysis, still being actively followed either as inpatients or outpatients at this hospital. Others were now residing in various parts of the country, there being followed by Veterans Administration installations or private physicians. A questionnaire was sent out to all in this latter group, which was designed to provide us with a reasonably complete picture of their current urologic status. These questionnaires, our own hospital records and x-rays and personal contact with all now hospitalized here or living nearby have provided the information presented in this paper.

The paper is not intended to present original, investigative work, but rather it is written as a sequel to the genitourinary study of these same patients 5 years ago. In order that a valid comparison of statistics could be made, the same arbitrary definition of terms used by Hutch and Bunts has been adopted for use in this study.

To correlate the clinical findings with the level of the cord lesion, only three divisions are used: cervical, dorsal, and lumbosacral. Injuries at the vertebral level of D-12 are included with the lumbosacral group, since a lesion there could and frequently does damage the bladder reflex centers in the sacral cord.

We have again classified the bladders of these patients as either "good" or "poor neurogenic bladders," and intend this division to apply only to the present bladder status, as based on the following arbitrary premise—that a good neurogenic bladder refers to one which empties no more often than every 2 hours, and must be able to retain its contents without leakage for that period of time under conditions of normal exertion and fluid consumption. It should, moreover, empty itself to the extent that the residual urine is under 100 cc.

Of the original 170 patients in the study of 5 years ago, we have been able to obtain the necessary clinical information on 134 for inclusion in the present followup. The remaining 36 either could not be traced by mail or failed to return their completed questionnaires.

It was found that 21 of the 134 reportable cases, or 15 per cent had died at some time during the past 5 years. Table 1 shows a breakdown of the deaths as to the immediate cause and the average time elapsed since injury. To place this mortality rate in the proper perspective, due consideration should be given to

Read at annual meeting, Mid-Atlantic Section of American Urological Association, Atlantic City, N. J. April 14–16, 1955.

TABLE 1

Deaths: Immediate Cause	No.	Average Yrs Since Injury
Renal failure	8	5 yrs. 6 mos.
Coronary occlusion	2	7 yrs. 3 mos.
Cerebrovascular accident	2	3 yrs. 2 mos.
Violent	4	5 yrs 9 mos.
Pulmonary embolus	2	7 yrs 1 mo
Pneumonia	1	26 yrs.
Infectious hepatitis	1	2 yrs 6 mos.
Undetermined	1	7 yrs 3 mos
Total	21	

TABLE 2. *Correlation of type bladder with level of lesion*

	C.C.	Inc C	C.D.	Inc D	C L S	Inc L S
Good neurogenic bladder (66)	3	7	23	3	13	17
Poor neurogenic bladder (47)	4	3	25	2	5	8
Total	7	10	48	5	18	25

Legend C.C.—Complete cervical; Inc. C.—Incomplete cervical; C D —Complete dorsal; Inc. D —Incomplete dorsal; C.L S.—Complete lumbosacral; Inc. L S.—Incomplete lumbosacral

the fact that approximately one-fifth of these deaths resulted from violence, rather than organic disease. As has often been shown in the past, renal disease again is found to be the chief killer, accounting for approximately one-third of the deaths if we exclude those due to violence. In one patient who died elsewhere, the cause of death is as yet unknown to us.

Of the 134 traceable paralyzed veterans, 113 are living and 66 of these, or 58 per cent now have good neurogenic bladders, as compared with 51 per cent good bladders 5 years ago. These cases as well as the 47 with clinically poor bladders are broken down according to the level of their vertebral lesion in table 2. It will be seen that 59 per cent of the cervical lesions, 49 per cent of the dorsal lesions, and 70 per cent of the lumbosacral have functionally good bladders at the present time. This high percentage of good bladders in the lumbosacral group is, we believe, due to several factors. First, it is rare to have a cauda equina injury so complete as to produce a denervated or autonomous bladder. Second, peripheral spasm, which is one of the chief antagonists of bladder training in lesions of the upper cord, is rare in conus or cauda equinal lesions. Third, abdominal muscles are preserved in low lesions and aid in voiding; and fourth, the low lesion usually permits greater awareness of a full bladder, which is beneficial in bladder training.

The vast majority of the 47 patients having clinically poor neurogenic bladders in this series have actually achieved a reflex type bladder. However, they must be classified as "poor reflex bladders" because they fail in one or more of the

TABLE 3 *Factors chiefly responsible for poor bladder status*

Factors	No	Percent
Spasm	23	49
Short cycle	20	43
Contraction? (small capacity)	18	38
High residual	11	23
Leakage	10	21
Lower tract complication	6	13
Lack of co-operation	3	6

requisites for a good bladder status. For example, many of these are unable to retain urine for 2 hours because of small bladder capacity, or because spasm will cause the bladder to "kick-off" before capacity is reached. Ten of these patients with poor bladders have never achieved a reflex bladder; six of these have responded to every voiding trial by going into complete retention. This situation has persisted in spite of many attempts to correct it by tidal drainage, bladder neck resections and nerve blocking procedures. The other four could not be trained because of complete incontinence, describing urination as a constant dribble. Since this latter group all have low spinal lesions, it is postulated that injury of the sacral reflex center of the pudendal nerves may have resulted in flaccid paralysis of the external sphincter.

Table 3 lists the factors found to be chiefly responsible in the persistence of a poor bladder status among these 47 patients. As previously mentioned, peripheral spasm is the most common offender. In those patients having a short voiding cycle, spasm was usually the reason for the inability to retain urine 2 hours. Lower tract complications, such as periurethral abscess with its sequelae, fistulas and urethral diverticula were the chief causes of failure to develop good bladders in only 6 patients. Five of these now use a permanent perineal catheter, after many recurrences and attempted unsuccessful surgical repair of fistulas. The other patient had a periurethral abscess about 6 months ago, and a urethral catheter has only recently been restored. As soon as his perineal urethrostomy has healed sufficiently, it is hoped that he will return to the good reflex bladder status previously achieved. The incidence of lower tract complications on our cord injury service is now very low, a fact which we attribute to the use of small soft rubber (No. 16–18 Foley) catheters, with constant catheter care by a staff of trained technicians.

ANATOMICAL AND FUNCTIONAL CHANGES IN THE UPPER URINARY TRACT

Three hundred ninety-three excretory urograms performed during the past 5 years on the 113 living patients were analysed. Each urogram was classified according to presence or absence of dilatation and calculi, and the function of each kidney assessed in terms of promptness of appearance of the contrast medium. The urograms were further classified according to the elapsed time since injury to the nearest 6-month interval and the information was then portrayed graphically. In order to graph the net functional loss during these past 5 years, appearance of contrast medium in the 5-minute film was classified "excellent," classified "good" if first seen in the 15-minute film, "fair" if first seen in the 30-minute film, and "poor" if no excretion could be seen in 30 minutes.

Arbitrary numerical values were then assigned as follows: Excellent, 0; good, 1; fair, 2; and poor, 3. By adding these figures and dividing by the number of kidneys reviewed, an arbitrary figure, called the "index of lost renal function" was reached which increased as renal function decreased, and could then be plotted at 6-month intervals on the graph along with the anatomical changes. Every effort was made to evaluate these x-ray findings in the exact terms used by Hutch and Bunts in 1949, so it is hoped that the graphs represent a 5-year projection of the figures presented in the earlier review. Our graphic portrayal of the second 5 years of upper urinary tract changes in the entire group is shown figure 1. In order to give continuity to the picture throughout the entire 10 years that these patients have been followed, Hutch's graph of the first 5 years following injury is reproduced here alongside our graph of the second 5 years. Reflux, of course, was determined by cystography, which was not carried out routinely except where frequent "flare-ups" of chills and fever, or the appearance of dilatation in kidney pelves and ureters suggested the possibility of reflux. A total of 33 cystograms were performed at this hospital on these particular patients during the past 5 years, and the graph shows a gradual rise to an incidence of 18 per cent in the tenth year, from the 10 per cent incidence found by Hutch and Bunts at

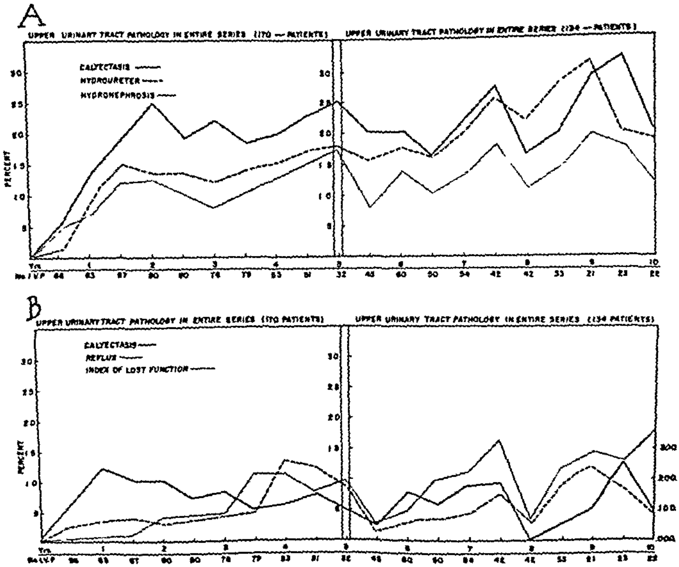

FIG. 1

the end of 5 years. The index of lost function also continues to rise during the second 5 years, as does the incidence of hydroureter and calyectasis, whereas no significant trend in hydronephrosis is apparent.

We believe that the occurrence of reflux is the most significant factor in the changes that occur in these patients' upper urinary tracts during the second 5 years. We know that calculi and acute pyelonephritis are the chief agents of renal destruction during the first few years, the infection usually resulting from the necessity of using a catheter early in the clinical course. But the late appearance of reflux on the scene results in progressive dilatation of the ureters and a fresh attack of pyelitis each time the regurgitation occurs. These repeated assaults by infection result in gradual blunting of the calyces, without producing hydronephrosis that would occur if an obstructive process were responsible.

Figure 2 shows the incidence of upper tract changes occurring in the 66 patients who have good neurogenic bladders. Of particular interest is the revelation that of 26 cystograms performed on this group, none has shown reflux during the second 5 years of this followup. That finding, with the presence of a high percentage of reflux in patients with poor neurogenic bladders, is consistent with our current concept of the pathogenesis of vesicoureteral reflux. This concept has recently been well described by Hutch and is essentially that it is the chronically inflamed, trabeculated bladder that gradually becomes thinned and sacculated around the intramural portion of the ureter, causing incompetency of the normal valve-like

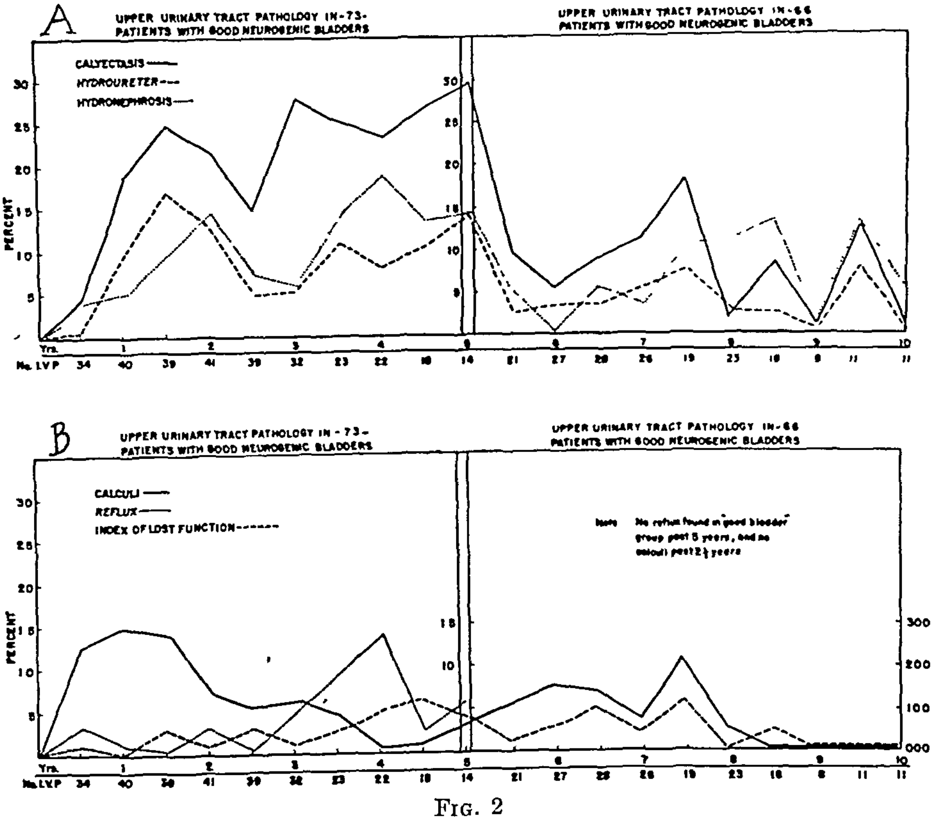

FIG. 2

action and allowing reflux. This type of bladder, of course, may result from the prolonged presence of an indwelling catheter, calculi, and recurrent infection. In addition, we believe that detrusor decompensation is greatly hastened in many patients by the constant triggering of the bladder reflex by spastic impulses arising in the hyperirritable segment of the cord distal to the injury, as suggested by Scarff and Poole.

A plastic reconstruction of the ureterovesical junction devised at this hospital by Hutch in 1949 has been performed on 9 of the patients in the present series: 5 unilateral and 4 bilateral repairs. Each had shown unilateral or bilateral reflux on three or more interval cystograms prior to surgery. In only one of these patients has the operation failed to prevent subsequent reflux during a postoperative period now averaging 33 months, and none has shown postoperative x-ray evidence of ureteral stricture or progression of renal impairment.

Figure 3 shows the late changes in the upper tract of those patients with poor neurogenic bladders. Comparison of these figures with those illustrating the status of the upper tracts in the patients with good bladders presents a striking contrast and illustrates much better than words the truth in the expression "in

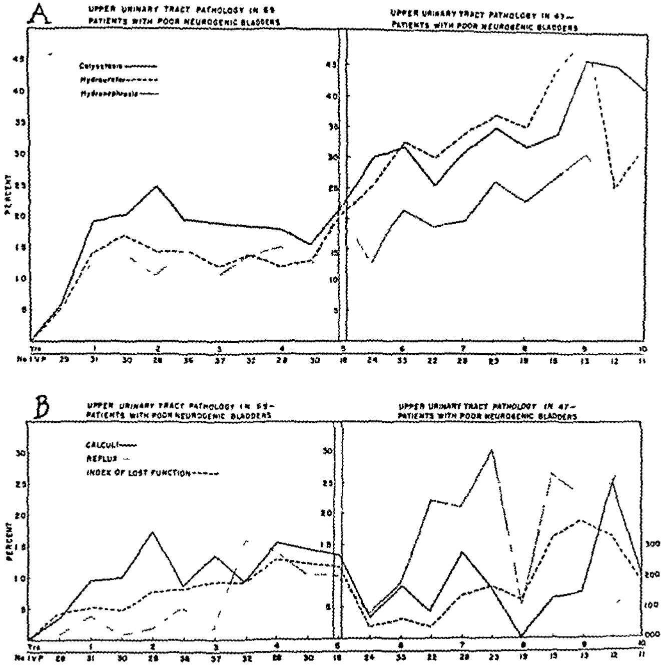

FIG. 3

the paraplegics, as the bladder goes, so go the kidneys." In general, this series of line graphs shows that those patients who achieved and have maintained a functionallly good neurogenic bladder, have had no reflux, few calculi, and renal integrity has been maintained during the second 5 years at nearly as good a level as was present at the end of the first 5 years following paralysis. In contrast, the patients with poor bladders show definite progressive increase in the depreciation of the structure and function of their upper urinary tracts.

SUMMARY

This study is based on urological data collected on 134 cord injury patients of 170 patients whose long term followup was initiated by Hutch and Bunts 5 years ago. Twenty-one of the 134 traceable patients are dead, making the 10 year mortality rate 15 per cent. The 113 living followups average 9 years since onset of paralysis.

Clinically, good neurogenic bladders are found in 66 at the present time, poor neurogenic bladders in 47 patients. A number of the factors responsible for poor bladder status have been discussed, and a study of the anatomical and functional changes in the upper urinary tracts of these patients during the second 5 years following injury has been presented. The correlation between these upper tract changes and the type of bladder function present has been graphically demonstrated. It is hoped that this group of paralyzed veterans will be the subject for continued followup studies, and that a 15-year analysis will be done in 1959.

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The Journal of Urology
Vol 75 No 1 January 1956
Printed in U. S. A.

A MODIFIED POSITION FOR TRANSURETHRAL RESECTION OF BLADDER TUMORS IN WOMEN

REGINALD A. HANCOCK

The removal of bladder tumors with the resectoscope has definite advantages over those open surgical methods One can remove tumor down to what appears to be normal musculature revealing the interlacing muscle bundles The periphery and depth of the area are resected, the tissue examined for evidence of tumor In those bladder tumors that are located high in the dome or on the anterior wall, we are unable to do as complete a resection unless the assistant, resident, or nurse pushes down on the suprapubic area to bring the tumor within reach of the resectoscope This is quite awkward and difficult for the operator

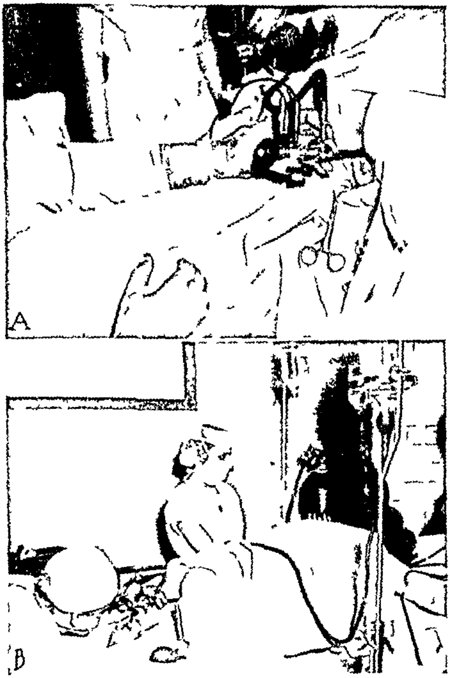

Fig 1

Read at annual meeting Southeastern Section of American Urological Association, New Orleans, La March 20–24, 1955

With the patient on her abdomen, under pentothal anesthesia, and her legs separated so as to rest on padded tables, the operator is in a comfortable position to resect the tumors on the anterior bladder wall (fig. 1, *A*). In this position, tumors on the anterior wall of the bladder are as easily resected as tumors on the floor of the bladder with the patient in the usual position for a transurethral resection (fig. 1, *B*). This position has not been applicable to the male patient.

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THE JOURNAL OF UROLOGY
Vol 75, No. 1, January 1956
Printed in U.S.A.

VESICOVAGINAL FISTULA

BAHIJ S. AZOURY, PETER L. SCARDINO AND CHARLES L. PRINCE

In A. J. Skene's book on *Diseases of the Bladder and Urethra in Women*, published in 1887, the recommended treatment for intractable cystitis in the female is the construction of a vesicovaginal fistula in order to divert the urinary stream. "But the main difficulty," states Skene, "has been to keep the incision open." This quotation was made by Beneventi and Gissen[1] in a recent paper in which they reported a case of complete healing of a large vesicovaginal fistula following hysterectomy for fibroids by simply placing the patient in a prone position with an indwelling catheter.

Occasionally a vesicovaginal fistula may close by simple catheter drainage. However, it may become a challenging problem to the urologist and the gynecologist. More than one trial is sometimes made to close a vesicovaginal fistula. With each subsequent attempt the procedure becomes more difficult and the chances of cure smaller. It is impressive to note that patients operated on once have the highest rate of cure. Those cases which cannot be closed successfully eventually become the victims of a urinary stream diversion procedure. This is not to be considered a success indeed! It is the beginning of a series of unphysiological processes resulting in undesirable complications with which every urologist is familiar.

Whereas in the past vesicovaginal fistulas occurred after prolonged and difficult labor or obstetrical mismanagement, the most common cause at present appears to be pelvic surgery and irradiation therapy. It is not difficult to understand the ease with which a vesicovaginal fistula may occur from such procedures. Anatomically, the base of the bladder, directly above the trigone, lies in contact with the upper portion of the anterior vaginal wall. Injury to the bladder at that point of contact between it and the vagina, whether by an instrument, a suture or interference with the blood supply, may result in the development of a fistula. Unless further improvement is achieved in the art of irradiation of pelvic neoplasms, vesicovaginal fistulas will continue to occur. These fistulas are the ones most likely to persist following attempts at repair. They usually represent the necrosed central portion of a much larger zone of ischemic tissue which heals very poorly.

The interval between the occurrence of the fistula and the time of closure is of vital importance in determining the success of the procedure. Most of the failures encountered are invariably due to the brief interval allowed for postoperative repair of the damaged tissues. Three months following the initial injury or failure at repair should elapse before undertaking closure of a vesicovaginal fistula.

The routes employed in the repair of a vesicovaginal fistula are either vaginal or transvesical or a combination of both. Each method has its advocates.

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of American Urological Association, New

.tive cure of vesicovaginal fistula. J. Urol.,

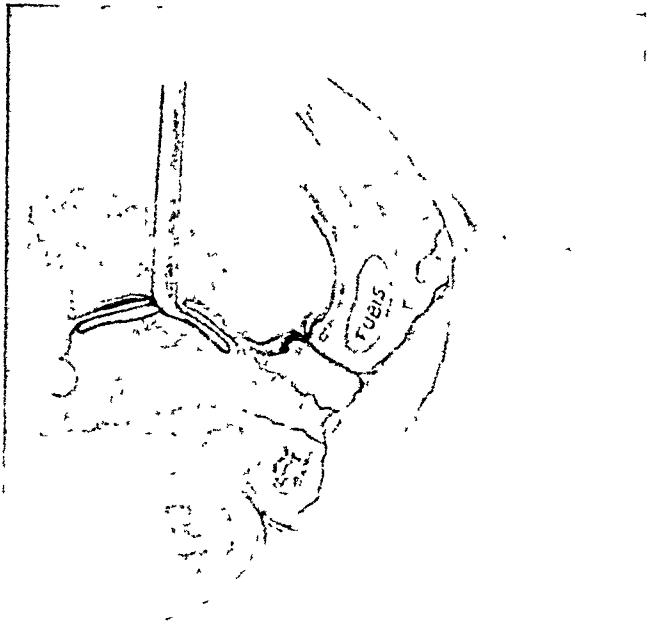

FIG. 1

The literature is replete with reports which present a large series with high percentages of success showing the adequacy and the advantages of the method in question.[2, 3, 4] The transvesical procedure was used in the cases reported below. With this approach the tissues at the margin of the vesicovaginal fistula can be adequately mobilized into separate layers of bladder mucosa, muscularis, and vaginal wall to permit their individual closure. The ureteral orifices which are usually in close proximity to the vesicovaginal fistula can be readily identified and, if necessary, catheterized while the dissection is carried out and closure performed. This is not feasible with the vaginal approach. The exposure obtained by the transvesical route is far more adequate than the vaginal one.

Access to the vesicovaginal fistula is rendered more feasible by the use of a traction device. Various types of hooks, forceps and tractors have been described.[3, 5, 6] The Young's prostatic tractor has been used for fistulas of 1 cm. or more in diameter (fig. 1). With the bladder opened in its anterior wall the tractor is inserted through the fistula and opened out. By gentle traction on the tractor the floor of the bladder and the orifice of the fistula are elevated to a convenient and accessible position. This traction is maintained while the dissection is carried

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out. Satisfactory exposure of smaller fistulas may be gained by the use of lead shot of varying sizes attached to a silk suture which has been introduced into the bladder from the vagina. Tension applied to the bladder end of the suture results in the tenting-up of the fistulous opening and thereby permits easier dissection of the tract. Closure is accomplished in layers using interrupted sutures

TABLE 1. *Results in 14 cases of vesicovaginal fistula*

Case	Age	Etiology of Fistula	Location & Size of Fistula	Previous Attempts at Closure	Time of Repair	Method of Management	Results
(1)	41	Carcinoma of cervix treated by radium & x ray therapy	In trigone 1 cm Rectovaginal fistula	None	6 wks	Bilateral cutaneous ureterostomy	
(2)	40	Carcinoma of cervix, treated by radium application on 3 occasions	Above trigone. 8 x 3 mm	None	3 mos	Transvesical closure	Cured
(3)	28	Hysterectomy for unknown cause	Above trigone 1 cm	None	3 mos	Transvesical closure	Cured
(4)	40	Forceps delivery, extensive avulsion of urethra, floor of bladder & vagina	Most of floor of bladder 8 cm	None	5 mos	Transvesical closure Reconstruction of sphincter & urethra Failure Bilateral ureterosigmoid	
(5)	42	Hysterectomy for unknown cause	Above trigone Pin point	Vaginal repair	4 yrs	Transvesical closure	Cured
(6)	40	Hysterectomy for unknown cause	Above trigone 2 5 cm	None	3 mos	Transvesical closure	Cured
(7)	40	Difficult labor & delivery with traumatic absence of urethra & bladder neck	In trigone and bladder neck Very extensive	None	7 yrs	Bilateral ureterosigmoidostomy	
(8)	40	Hysterectomy for unknown cause	In trigone 3 mm	None	4 mos	Transvesical closure	Cured
(9)	38	Forceps delivery	In trigone 1 cm	Vaginal repair	3 mos	Transvesical closure	Cured
(10)	27	Hysterectomy for unknown cause	Above trigone 10 x 3 mm	None	3 mos	Transvesical closure	Cured
(11)	29	Hysterectomy for unknown cause	Above trigone 2 x 3 mm	3 vaginal repairs	3 mos	Transvesical closure	Cured
(12)	43	Hysterectomy for unknown cause	Above trigone 0 5 cm	None	3 mos	Transvesical closure	Cured
(13)	40	Carcinoma of cervix treated by radium & x ray therapy	In trigone 1 5 cm	None	6 wks $1\frac{1}{6}$ yrs	Two transvesical closures Failures Bilateral ureterosigmoidostomy.	
(14)	35	Hysterectomy for fibroids	Above trigone 1 cm	Vaginal repair	3 mos	Transvesical closure	Cured

of chromic catgut left long for traction. After placing the first few sutures the traction device is removed and the accessible position of the fistula is maintained by the traction sutures. The bladder is closed around a de Pezzer catheter. A 18F Foley urethral catheter is inserted and the patient placed in bed on her side or in the prone position. These measures insure continuous drainage and also prevent urine from leaking upon the suture line. Indwelling ureteral catheters for supplementary urinary drainage have not been used. They block easily and the urine invariably flows around them. They require constant attention and only add to the already existing nursing problems.

Fourteen cases of vesicovaginal fistula are reported (table 1). These patients ranged in age between 27 and 47 years.

Eight cases resulted from pelvic surgery, three from irradiation therapy for neoplasm of the cervix and three as a result of obstetrical difficulties. The location of the vesicovaginal fistula was in or adjacent to the trigone in all cases. The size ranged between a few millimeters to as much as 8 cm. in diameter.

Of the 14 cases, four had undergone previous attempts at closure by the vaginal technique and failure had resulted (cases 5, 9, 11 and 14). Case 11 was subjected to three such attempts. All were cured by the transvesical closure.

Twelve cases were operated on by the transvesical technique for a total of 13 operations. Ten were cured. Of the 2 failures, one patient (case 13) had an extensive irradiation burn of the bladder and vagina. Two attempts at transvesical closure resulted in failure. The other patient (case 4) had severe avulsion of the urethra, sphincters, floor of the bladder and anterior vaginal wall. The fistula measured 8 cm. in diameter. Besides closing the fistula an extensive repair procedure of the urethra and sphincters and reconstruction of the vaginal wall were undertaken. In retrospect, it was believed that the repair was not justified except the reconstruction of the avulsed anterior vaginal wall from the labia. These 2 patients were eventually subjected to bilateral ureterosigmoidostomy. The two other patients in this series who underwent a urinary stream diversion procedure were handled as such from the start. Case 1 had a vesicovaginal as well as a rectovaginal fistula resulting from irradiation for carcinoma of the cervix. A bilateral cutaneous ureterostomy was performed. Case 7 is similar to case 4. As a result of difficult labor, the urethra and most of the bladder neck were absent besides the extensive vesicovaginal fistula. A bilateral ureterosigmoidostomy was done.

SUMMARY

A series of 14 patients with vesicovaginal fistula is presented. The etiology, pathological anatomy and treatment are discussed. Emphasis is placed on the transvesical technique as a very satisfactory and highly successful method of closure. The operative technique and the postoperative care as employed in this study are outlined. The results of treatment are discussed and considered encouraging.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 1, January 1956
Printed in U.S.A.

THE USE OF THE VAGINAL BALLOON CATHETER FOR THE CONTROL OF STRESS INCONTINENCE IN WOMEN

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The introduction of a balloon catheter into the vagina is a simple nonoperative technique which may be used in the treatment of certain selected patients with urinary stress incontinence. It is particularly applicable in elderly patients who are considered poor surgical risks or in whom conservative measures or surgery have failed.

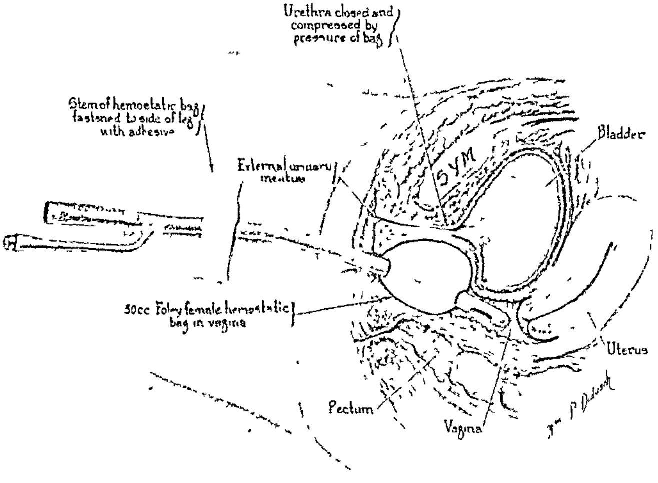
Urethra closed and compressed by pressure of bag
Stem of hemostatic bag fastened to side of leg with adhesive
External urinary meatus
SYM
Bladder
30cc Foley female hemostatic bag in vagina
Uterus
Rectum
Vagina

FIG. 1

A 24F Foley catheter with a 30 cc bag is used (fig. 1). It is important that the catheter be patent at all times to allow satisfactory drainage of the vaginal secretions. We have found that distension of the balloon from 25 cc to 40 cc is satisfactory in most patients, although this is an individual problem. Overdistension of the balloon may produce rectal distress and may interfere with urination. The catheter should be changed at least every four weeks and discarded. Used catheters will invariably break so that a new catheter should be employed each time.

We have used this method to control stress incontinence in one patient for over three years with excellent results. In other cases the prime difficulty en-

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Abstract of paper read at annual meeting, Mid-Atlantic Section of American Urological Association, Atlantic City, N J April 14-16, 1955 countered was the maintenance of the balloon in its vaginal position. A tight introitus is essential. Through the co-operation of C. R. Bard, Inc., we are endeavoring to design a balloon type catheter or support which will overcome this difficulty.

This is not an original technique but one which we feel is novel and worthy of a trial. Those of us who treat this unfortunate condition realize that the successful application of a simple procedure, such as the one described, will be rewarding to the physician and patient alike.

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The Journal of Urology
Vol 75 No 1, January 1956
Printed in U S A

A CLINICAL STUDY OF URETHRAL INJURIES

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In the past 10 years (1945–1954) we have treated 220 cases of urethral injuries, 70 of which were open injuries (war wounds) and 150 closed injuries The great majority of the open injuries were encountered during the war (1944–1945) and only exceptionally in later years Closed injuries, on the other hand, were rare during the war (traffic accidents in the transports) This proportion was as follows

1) During 1945	open injuries	55 cases
	closed injuries	15 cases
2) From 1946 to the end of 1954	open injuries	15 cases
	closed injuries	135 cases

It should be mentioned here that most of open injuries met with after 1945 (11 of the total of 15) had in fact been inflicted during 1945, but were delivered to us for treatment much later because of the delayed consequences of the injury (stenosis of the urethra)

A part of our experience has already been published The relatively great number of urethral injuries treated at our clinic represents a fairly accurate incidence of such injuries for a population of 8 million inhabitants, for all these cases from the entire territory inhabited by this population were sent to us for treatment The publications written in conjunction with our late chief surgeon, Professor Kojen, influenced other groups so that practically all injuries of this type were sent to our clinic

The pathologic anatomy, etiology and treatment of these injuries are discussed in the standard textbooks of urology and in more recent years in publications by Young, Kimbrough, Poole-Wilson, Sabatini, Clarke and Leadbetter, Culp et al , Graham, Lewis, McCague and Semans, Robinson et al , Reynolds and Vermooten

OPEN INJURIES

Etiology These injuries were caused a) by wounds due to rifle or pistol bullets in 61 cases, b) wounds due to explosive weapons in 8 cases, c) wounds due to pointed weapons (stabs) in 1 case This proportion, however, is unreal as the majority of those wounded by explosive weapons succumbed before reaching our clinic

Anatomy In 12 cases, the bullet had remained in the body (17 per cent) so that there was no exit wound In our series of cases, wounds above the pubic bones were rare, as these high wounds were connected with serious injuries to the intestinal organs causing, in many cases, the death of the wounded The entrance wound was most frequently near the urethra, and in some cases at a greater distance from it The exit wound was found in the gluteal and perineal regions, or

Accepted for publication June 14, 1955

near the urethra. As a curiosity we had one case with the entrance wound in the very meatus of the urethra (the exit wound was in the sulcus glandis).

The wounds on the urethra were located as follows:

a) pars pendula and pars scrotalis urethrae	30
b) pars bulbaris urethrae	8
c) pars membranosa urethra (or including also part of pars bulbaris)	12
d) pars membranosa and pars prostatica	20

Open injuries feature a relatively great frequency of lesions of the scrotal and penile parts of the urethra (43 per cent), while in the case of closed injuries, these parts are seldom affected.

Injuries to the surrounding bones were present in 32 cases (lesio ossium pelvis). However, if we consider only the lesions of the deep urethra (pars membranosa and pars prostatica), it will be found that they were practically always accompanied by injuries to the bones (excepting 2 cases for which no data are available). Injury to the bone is of great importance as it can result in prolonged osteomyelitis with delay in healing of the urethra. Osteomyelitis promotes the appearance of calculosis later in these immobilized patients, particularly as the injured urethra offers the possibility for an ascending infection. Out of 102 open injuries of the urinary tract, 8 were of the kidneys, 4 of ureters, 20 of the bladder and 70 of the urethra; we have had 13 cases in which calculosis occurred as a complication. Of these 13 cases of calculosis, 8 resulted from urethral injuries (11.4 per cent).

The bladder was injured (in addition to the urethra) in 5 cases (7 per cent). The rectum was injured in 12 cases (17 per cent). This percentage, however, rises to 36.9 per cent if only injuries to the deep urethra are taken into account. The testis was injured in 8 cases (11.4 per cent); incidentally, before admittance of these wounded to our clinic, castration had been performed in 3. This is, undoubtedly, too radical therapy in view of the possibility of healing of such injuries; however, late atrophy of the testis due to injury of its vessels by bullets occurred in 3 cases.

Periurethral changes are of great importance. Periurethral hematoma, which usually accompanies injury, can compress and disturb the urethra and make the injury appear more serious than it really is. The possibility of infection of such a hematoma or of the periurethral space is present even if the hematoma is small, this infection being caused by the foreign body and by the flooding of this space with infected urine. Thus a fistula forms later with recesses of varying shapes, rendering healing and closure difficult. Suppuration of such a hematoma causes much more serious stenosis of the urethra than would occur otherwise following injury. Hence, even minor injuries of the urethra may be accompanied by serious impenetrable stricture. In some cases the stricture can be dealt with by simple removal of the periurethral scar, the urethra, when freed of the surrounding scar, becoming permeable. It is possible that periurethral retraction alone will lead to angulation of the urethra, rendering it impassable to any filiform sound, although urination is easy (2 cases). Simple separation of the angulated urethra from the bone may lead to good results (Petkovic, 1950). In order to prevent strictures and perineal fistulas, speedy and correct surgical treatment of such injuries is entirely justified provided it is combined with correct drainage of the hematoma and proper urinary drainage Micturition after the injury is of great importance, immediately following the trauma

A) In 27 cases, micturition was spontaneous, namely, through the meatus of the urethra, and in 20 cases through the wound near the urethra (entrance or exit wound) In the latter, some of the urine at times also passed through the meatus Of these 20 cases, in which micturition took place through the wound, it was later necessary to carry out a cystostomy in 12 cases

B) Acute and complete retention of urine was present in 43 cases Urinary drainage in these cases was accomplished in following ways In 12, an indwelling catheter was necessary, in 6 cases, intermittent catheterization was sufficient In 25 cases urgent cystostomy was necessary

Of the 70 open injuries of the urethra, cystostomy was performed, early or late, in 45 cases, or 64 per cent This illustrates the importance of cystostomy for the diversion of urine Although we do not recommend cystostomy as a routine practice, since it can be avoided with minor injuries (especially of the anterior meatus) provided there is spontaneous micturition, one should nevertheless not hesitate also to perform a cystostomy if a larger injury is involved Cystostomy should be done when the retention continues, when there is considerable trauma to the perineum and particularly when any complication follows the injury, as infection or extravasation Cystostomy is also necessary if repair of the deep or bulbar urethra has to be carried out

An indwelling catheter has its advantages, but on the other hand, its disadvantages as well One of the disadvantages is the possibility of periurethral infection and the development of a fistula Its advantage consists of the possibility of avoiding cystostomy (incomplete tear) and in addition, the catheter acts like a splint around which a wider scar forms In injuries of the deep urethra, the indwelling catheter may promote periurethral suppuration and as a result, a dense periurethral infiltration Thus a hard, dense stricture may result (developing later into stenosis difficult to dilate) In injuries of the scrotal and penile urethra the indwelling catheter promotes the formation of a fistula due to the proximity of the urethra to the surface of the penis However, the use of antibiotics and proper care and frequent changing of catheters will minimize periurethral suppurations which would otherwise be very harmful

Diversion of urine in operations for repair of the urethra was done in all cases by cystostomy Cystostomy was done in 33 cases of complete repair of the severed urethra, and in 8 cases of partial repair The latter were operations on the prostatomembranous part of the urethra With the cystotomy drainage in cases of complete repair of the urethra an indwelling catheter was not employed because it was unnecessary as a splint In operations on the bulbomembranous urethra where only partial union could be accomplished the indwelling catheter was inserted as a splint In the cases of complete urethrorrhaphy, there was reason to fear that a catheter which would be introduced after a few days might cause "false route" and therefore a "conductive thread" was employed extending through the urethra and out alongside the cystotomy in order to be able to reinsert a catheter later. Perineal urethrotomy for urinary diversion was not used by us, although it had been done in 3 patients before arrival at our clinic. Although urethrotomy is recommended in many of the older textbooks, this method does not appear to us as being very suitable due to the difficulty of maintaining the necessary drainage.

Intermittent catheterization and permanent catheters have been used in cases of repair of small fistulas after injuries (8 cases) and transpositions of the urethra through the meatus (3 cases). The retention catheter was used for only short periods, as longer application would favor dehiscence of the wound.

Immediate repair of the urethra is not advisable in the active war area, especially not in medical outposts. This was also the opinion of P. Wilson based on experience during the Italian campaign (1944). The reasons are the following: First of all, there may be multiple injuries requiring immediate surgical attention, and no time should therefore be lost with the complicated operation on the urethra. Secondly, the surgeon would have to deal with very contused tissue and the possibility of slough of the sutured area and of thus sacrificing more of the urethra than would be necessary at a later time. Thirdly, such an operation calls for a good surgeon who may not always be present in the first combat lines. And fourthly, the operated patient requires correct urological care. In view of the speed with which casualties can nowadays be transported to hospitals in the interior, and the use of antibiotics, indications for urgent repair of the urethra in wartime can be extended. Nevertheless, immediate attention must be given to preliminary treatment of the wound and urinary drainage. We had met only 2 patients in whom we considered that immediate urethrorrhaphy was needed. However, it had been done in 6 cases by surgeons working in forward medical stations, and the results in these cases were poor.

NONOPERATIVE TREATMENT

This category comprises those cases treated without operation on the urethra, although in some of them cystostomy had been done as urgently required for urinary drainage. Treatment consisted in systematic calibration of the urethra. Twenty-six casualties come into this group as follows: a) dilatation only in 8 cases; b) cystostomy and dilatation in 13 cases; c) in 5 cases micturition was normal and the patients declined further treatment. As can be seen, a considerable percentage of the injuries (39 per cent) was treated without urethral operation. This shows that quite a number of casualties were of lesser degree and that in certain cases of partial injuries of the urethra good results can be obtained through dilatation only, as ascertained by subsequent control of our patients.

OPERATIVE TREATMENT

We did not use the Pasteau-Iselin method as we considered that it had no indications anymore today, or in other words, that it is inferior to the methods used by us. Nor did we use, in cases of open injuries, internal or external urethrotomy, although we applied it in some rare cases of closed injuries. The reason for avoiding urethrotomy as much as possible lies in the fact that in urethral injuries periurethral changes with remarkable cicatrization are very significant, whereas in gonorrheal strictures the changes are mainly of an endourethral nature and thus the effect of urethrotomy is of more value. However, in cases of minor urethral injuries, where undilatable strictures occurred as a sequel, either internal or external urethrotomy can be done with some success if the sound is absolutely impassable or excision of the periurethral cicatrix is necessitated, depending on the location of the stricture and caliber of the urethra.

The following operations were done: a) Transposition of urethra through meatus. The method is identical with the Beck-von Hacker method applicable to glandular hypospadias. It may be resorted to in injuries proximal to glans only. This method consists in having the prepared urethra brought through the old meatus and sutured in place. Cystostomy is unnecessary and the patient either retains a catheter for 2 or 3 days or micturition is spontaneous without a catheter and in some cases of retention intermittent catheterization may be necessary for a few days. We have operated on 3 cases with good results. b) The suture of the lateral defect of the urethra or fistulous tract; 8 wounded were operated on with good results. c) Complete urethrorrhaphy following the classic technique of Marion and McGowan was done in 25 cases. This is the ideal operation for severe injuries and the results were excellent where it was correctly applied. In these cases complete excision of the periurethral scar and fistula was mandatory following a careful preoperative removal of infected tissue and with control of periurethral and systemic infection by antibiotics. Defects up to 8 cm. long may be bridged by mobilization of the two ends of the urethra. The retention catheter was not necessary where operation was properly done for injuries of the bulbar and scrotal urethra. It was necessary in injuries of the membranous urethra where only incomplete urethrorrhaphy could be done. d) Incomplete urethrorrhaphy was done in 8 cases, all of them involving injuries of prostatomembranous urethra. In these injuries the two ends of the urethra could not be completely reunited as was done with the injuries of the anterior urethra. In these, a catheter was introduced in a retrograde manner through the cystotomy wound and the urethra splinted over it, the catheter then left indwelling. As much of the surrounding tissue as possible was sutured over the catheter leaving the indwelling catheter as a splint, so that a new urethral canal could be formed around it. The severed ends of the urethra were thus near to each other or almost approximated rendering the results relatively good. They were not so good, however, as those obtainable by complete urethrorrhaphy, where complete excision of the scar and fistula could be done and anatomical reunion of the cut ends, as in the McGowan operation.

URETHRORECTAL INJURIES

These were 12 in number and have been reported previously in publications jointly with Professor Kojen. Treatment of these injuries was as follows:

(A) Palliative operations cystostomy and debridement of wound, 3 cases;

(B) Dedoublement (debridement) and splitting of perineum and suture of rectum, 3 cases;

(C) Dedoublement and splitting of perineum, suture of rectum and urethrorrhaphy, 3 cases.

(D) Dedoublement and splitting of perineum, suture of rectum and restitution of urethra under application of indwelling catheter—incomplete urethrorrhaphy, 3 cases.

Urinary drainage was provided for as follows:

(A) In 7 cases by means of cystostomy; (B) in 3 cases by means of indwelling catheter; (C) in 2 cases urine was discharged per anus. Colostomy was done only in 2 cases, and it is our belief that it should not be used as a rule but only in cases of major destruction of urethra and especially of destructions in retrorectal region.

In urgent cases it is necessary, above all, to attend to the area of the injury, and then to provide for urinary drainage by cystostomy in most cases. In combined injuries of the urethra and rectum the peritoneum or intraperitoneal organs may also be injured (1 case of ours) in which case intraperitoneal intervention is also required.

In cases seen late it is of imperative necessity in treatment of the fistula to apply the classic perineal dedoublement or mobilization of rectal mucosa (Young and Stone) and a sufficient mobilization of rectum, so as to enable the defect of same to be sutured without tension. Sometimes nothing is to be done on the urethra if there is but a small lateral defect. If the destruction of the urethra is considerable, urethrorrhaphy must be done with or without use of indwelling catheter.

Mortality. There was no operative mortality. Three wounded died of multiple injuries and were not operated on. One patient died years after severe urethral injury which did not heal. Death was due to prolonged pyelitis, cystitis and chronic urinary retention.

CLOSED INJURIES

The various mechanisms of the closed injuries of the urethra were as follows:

A) Contusion of pubic bones due to crushing injuries, 30 cases.

B) Traffic accidents, 35 cases.

C) Striking upon any object in forked posture, fall from above, falling into a shaft or pit, 68 cases.

D) Blow against perineum, 10 cases.

E) Blow against the urethra, against pars penalis urethra, 2 cases.

F) Traction of penis in erection, 1 case.

G) Intraurethral injury, by metallic catheter, 4 cases.

H) Obscure cause of injury, 1 case.

It is rare for the urethra to suffer injury following injury to the penis by a blow against the pars penalis but it occasionally occurs due to trauma to the perineum. Injury to the urethra while penis is in erection, as well as injury to the urethra due to endourethral manipulations are rare. The urethra was injured in most cases by direct injury to the perineum and this usually involved the bulbar urethra. Most of these injuries occurred as a result of falling into an open and unprotected shaft or pit or by falling from a moderate height on a cross-rod, bar or any other solid object Thus compressed between hip bones and the object encountered in falling, the urethra always ruptured in the bulbar portion, the rupture extending from the bulb to 3 cm distal The injuries incurred were frequently slight, sometimes very light and at times strongly marked, but partial and incomplete, following the classification of Marion This fact is of importance, because a relatively large percentage of injuries originating from falling in forked posture were not operated on, sometimes were not treated at all and the results were, nevertheless, good or even very good The posterior urethra was ruptured in major accidents, such as being run over, compression of pubic bones, fracture and divulsion of the pubic bones, with severe body injuries, all in traffic accidents The mechanism here is multiple, both direct and indirect, and injuries of urethra were associated with other major injuries of the body The mechanism of these severe injuries has already been mentioned The traction of ligaments (lig pubourethralia) owing to dislocation of broken or luxated fragments of bone was the cause of bursting of the urethra, and the destruction of urethra only in exceptional instances could be attributed to injury arising from the penetration of fragments directly into the urethra In such cases, the injuries of the urethra were serious

Anatomy The location of rupture of the urethra was as follows a) pars penalis, 5 cases, b) pars bulbaris, 84 cases, c) pars membranosa, 49 cases, d) pars prostatica, 12 cases (posterior urethra totaling 61) Pars penalis and pars bulbaris are always ruptured as a result of direct trauma to the urethra, pars membranosa and pars prostatica are ruptured by indirect trauma, viz , in cases of fracture of pubic bones and of luxation respectively This is of diagnostic but not also of prognostic significance, i e , this fact may determine the location of the rupture but not necessarily the degree and the fate of the rupture In only one of our cases was a fracture of pelvis and the rupture of bulbar urethra alike associated, except fractures of pubes and rupture of the bulbar urethra both around the fracture in this case Of 61 cases of rupture of the posterior urethra, the following injuries occurred fracture of the pubes in 49 cases, dislocation in 2 cases, temporary luxation in 1 case, fracture had probably occurred in 8 patients who came to the clinic long after the injury, and in 1 case the rupture was free of fracture In 2 of the 49 cases the fracture had been so severe that it resulted in a comminuted fracture of the pelvis In these cases, in restoring the continuity of the urethra, the bony callus which had formed was resected in part in order to allow a passageway for the urethra, 1 case published (Petkovic, 1950) Luxation of the symphysis is an exceptional cause of injury Temporary luxation of symphysis with return of fragments to normal position immediately after injury is also rare

Injuries to the anterior urethra were in most cases incomplete for the patient usually can void spontaneously or a catheter can readily be passed immediately In our series, incomplete injury occurred in 77, or 86 5 per cent of the cases, whereas complete occurred in 12, or 13 5 per cent

In injuries of the posterior urethra it is difficult to determine whether the injury is complete or incomplete. Digital exploration through the rectum may show that the prostate has been displaced high above by hematoma and separated from the anterior urethra, as established by Vermooten. Such evidence is rarely present. On the other hand, the inability to pass a catheter, the persistency of retention and even the presence of a large hematoma are no proof that the rupture is complete. There may be only an incomplete rupture with a deep compression of the urethra by the hematoma with displacement of the urethra. Following cystostomy and evacuation of the hematoma the catheter may be readily passed through the urethra either antegrade or retrograde. This indicates that the injury was probably an incomplete rupture of the urethra. In our 61 cases, 36 were incomplete ruptures, 59 per cent; and 25 complete, 41 per cent. This varies from previous teaching that complete ruptures are more frequent. This greater frequency of incomplete rupture of the urethra is important in treatment and prognosis since a good result may be anticipated in incomplete injuries without operative repair of the urethra and, in many cases, merely by the use of the indwelling catheter after the evacuation of the hematoma. In complete ruptures, however, an open operation is necessary. The urethra is reunited when possible whether seen early or late after the injury. The torn ends of the urethra are splinted over a urethral catheter and a partial union is made if it is not possible to effect a complete union. The reuniting of the cut ends is often difficult for the torn ends may be buried in the traumatized tissue and found only with difficulty. Complete rupture of the urethra should be repaired as soon as possible. When not possible after the injury to reunite the urethra immediately, both ends of the urethra should be located when possible, although this is often difficult. This should be done for the purpose of passing through a catheter and making adaptation sutures. A catheter should be passed either antegrade or retrograde before adaptation sutures are inserted, unless a complete urethrorrhaphy can be done with the enclosing to some extent of the two ends of the urethra. The occurrence of a periurethral hematoma is important for various reasons: first, due to compression of the urethra the hematoma may be the cause of urinary retention and of inability to pass a catheter which can later be readily passed after the hematoma is evacuated. Secondly, cicatrization of a larger hematoma, especially when it is infected, produces a dense periurethral scar, with an impermeable stricture. Dilatation of the urethra is not possible and even internal urethrotomy can not be done. Thirdly, a large hematoma must be evacuated in order to prevent late scar formation and cicatrization and suppuration and also to allow proper drainage for an already existing suppuration. In rupture of the bulbar urethra the hematoma is in the perineum. In rupture of membranous urethra the hematoma is partly perineal, but is more frequently above the diaphragm of the pelvis, where it may be very large. In these cases drainage of the perineal hematoma may be done particularly for urinary drainage. In most cases, however, drainage of the high-lying hematoma above the pelvic diaphragm is carried out suprapubically. This is satisfactory even though it is uphill drainage. On the contrary, perineal drainage is absolutely contraindicated in extensive hematoma high up at the pelvic diaphragm because the infection is high above the pelvic diaphragm and will not drain well through the perineum (Wilson).

Severe periurethral and transurethral hemorrhage in urethral injuries is the exception in most cases. It occurred in only 3 cases of our series and urgent intervention was necessary for control of bleeding in 2 cases. In these the internal pudendal artery was torn and required ligation; the urethra was also completely torn and required complete urethrorrhaphy. In the third case the iliac vein was injured by a fragment of the broken pelvic bone and tamponade of the iliac vein by packing, together with a cystotomy were done. It is most important that there be free urinary drainage subsequent to the injury. It is, of course, necessary for the urgent care of the patient that urinary retention and the frequently associated urinary extravasation are controlled in order that the ruptured urethra will heal better and the prognosis will be better.

A) Spontaneous micturition occurred in 56 of 150 injuries, 37 per cent. This illustrates the frequency of incomplete rupture. It is also notable that a much higher percentage, 52 per cent, or 44 of 88 cases of rupture of the anterior urethra than of the posterior urethra, only 20 per cent, or 12 of 61 cases were able to urinate spontaneously. This indicates the greater frequency of incomplete rupture of the anterior, particularly the bulbar urethra, than incomplete ruptures of the posterior urethra.

In 19 cases out of those 56 previously mentioned where micturition was spontaneous after injury, we resorted to cystotomy either early or late, in 34 per cent of the cases only. We may, therefore, infer from this fact that if the patient has a spontaneous urination after injury it is most probable that in the course of treatment he will not require cystotomy or repairs of the urethra. This indicates that in a certain number of cases in our series, almost one-third, operation for repair in ruptures of the urethra could be avoided, i.e., we do not advise repair of the injured urethra in all cases but only in selected cases and varying with the extent of the injury.

B) Puncture of the bladder for the relief of urinary retention was done in 3 cases only, all prior to the arrival of the patients at our clinic. This procedure is rarely indicated. When necessary it is done on patients in whom a catheter could not be passed and a long interval had elapsed from the time of the injury and the arrival of the patient to the first surgical station. If the catheter is impassable and there is retention it is far better to resort to cystotomy than to trochar puncture of the bladder.

C) Indwelling catheter or periodic catheterization was instituted in 31 cases. The indwelling catheter is not favored by us. In cases of retention due to a minor injury, usually of the bulbar urethra, we prefer intermittent catheterization. The indwelling catheter was employed only infrequently in those patients with retention in whom a catheter could be passed easily and where no major hematoma was present and with no subsequent rise in temperature. Most of the patients treated by indwelling catheter had been cared for in this manner prior to arrival at our clinic. We do not favor the indwelling catheter for fear of periurethritis. However, suppuration should be avoided as much as possible, not only for the prevention of the periurethral infection ensuing immediately after injury, but also to avoid considerable cicatrization about the urethra as well. It is, however, notable that a substantial number of minor injuries of the bulbar urethra due to falling from a small elevation with either a moderate sized hematoma or no hematoma resulting are successfully treated with a retention catheter. These patients are mostly young, their general condition is good, and a speedy restoration of spontaneous micturition follows removal of the catheter. In major injuries, with fever, large hematoma and long-lasting retention, we do not recommend either the indwelling catheter or periodic catheterization but advise cystotomy as soon as possible. In ruptures of the posterior urethra, if the condition of the patient is good and there is no evidence of a large hematoma, and the urethral catheter can pass with ease, we recommend an indwelling catheter, for spontaneous micturition usually occurs very soon.

In 13 cases, or 42 per cent, of the patients treated with indwelling catheter or intermittent catheterization, as previously outlined, we found it necessary to do a cystotomy later. It should be remembered that most of these patients had been catheterized prior to their arrival at our clinic and a relatively small number of cystotomies were done in these patients which, of course, proved the accuracy of our indications for the use of an indwelling catheter or intermittent catheterization.

D) Urgent cystostomy was done in 58 cases, or 39 per cent. Urgent cystostomy is very useful in cases of rupture of posterior urethra or when urinary retention occurs, thus not only obtaining drainage of urine, but also evacuation of hematoma. Moreover, we attempt, at this time, to insert the urethral catheter which is often passed easily after the evacuation of the hematoma, although it was not possible to pass the catheter before this. Cystostomy is useful also in cases where injury of the intraperitoneal organs or injury of the bladder is suspected. It is thus possible to enlarge the incision and do a laparotomy and inspect the abdomen. In other cases, cystotomy also allows for the drainage of urine and splinting of the bladder and thus has a sedative action on the patient. We endeavor to avoid cystotomy on patients who are able to urinate spontaneously or in patients whose retention was readily overcome following a few repeated urethral catheterizations, or in whom urination was spontaneous after an indwelling catheter for 2 or 3 days. We did not hesitate, however, to procede with a cystotomy in all complicated cases. Cystostomy, in general, both urgent and late was done in 90 cases, or 60 per cent. This emphasizes its importance in ruptures of the urethra.

E) For deviation of the urine in repair of the urethra, cystostomy is absolutely necessary in cases of incomplete urethrorrhaphy and practically always where complete urethrorrhaphy is necessary. In incomplete urethrorrhaphy cystostomy must be done for the indwelling catheter is unsatisfactory. The catheter may become blocked and compromise the success of the operation. Also, when it is necessary to change the catheter some days later it is often passed only with difficulty. The passage of a catheter at a later date is made possible by using a conductive thread through the urethra extending out through the cystotomy wound. This is inserted at the time of the cystotomy and the urethral repair.

This makes changing of the catheter or inserting a new catheter very simple. Without this one may run the risk of a false passage which might readily compromise the results of the urethral repair.

In complete urethrorrhaphy we do not insert the urethral catheter except in cases where we are not certain of the accurate suture of the torn ends of the urethra. In some cases we inserted the thread which could be utilized some days later for passage of the urethral catheter. The cystotomy tube could then be removed. In selected cases, however, cystotomy may not be necessary in cases of complete urethrorrhaphy when antiobiotics are employed and in these cases, which must be carefully selected, the indwelling catheter alone can be used. In our last case, the patient was operated on successfully for complete urethrorrhaphy and a retention catheter only employed. However, in the vast majority of cases, the routine for urethrorrhaphy consists of doing a cystotomy for urinary drainage and avoiding an indwelling catheter due to the possible separation of the sutures and the formation of a fistula.

Methods of treatment. A) Dilatation of urethra was employed in 50 cases, or 33 per cent. As a method of treatment it was employed in cases involving a minor lesion of membranous or bulbar urethra, spontaneous micturition or early restoration of micturition subsequent to catheterization, absence of hematoma, absence of infection, easy catheterization. If the result of dilatation was not good, or it was not possible to dilate, or a marked tendency to new and early stenosis, we did not continue dilatation and did urethrorrhaphy instead. It is important to begin the dilatation quite early and to apply systematic dilatations until reaching the caliber of the urethra to be maintained (about 18 to 20 CH). Later, dilatations are done infrequently. It is remarkable to note the fact that, in certain cases of small lesions, a good result may even be obtained by a few dilatations and even without dilatation. (See next paragraph.) One of our patients has not been dilated for 18 years, and there was found, on subsequent examination, that nevertheless the urethra was easily dilated to 18 CH. There are some patients upon whom only a few dilatations had been undertaken after the injury without applying any more for months and years, and nevertheless there was found on examination an easily passable urethra. This can occur only in minor lesions with partial and incomplete ruptures. According to Marion, the bulbar portion of the urethra has a tendency toward contracture subsequent to injury, this being due to the presence of spongy tissue formed by the dense cicatrix. We also observed a frequent tendency to stricture of the bulbar urethra after injury which was subsequently dilated only with difficulty. However, in partial ruptures after a well done urethrorrhaphy, free of intense cicatrization, a very good result may be achieved even without additional systematic dilatations. Injuries of the membranous urethra have a tendency to an early stenosis immediately after injury or after incomplete urethrorrhaphy, but once the urethra has been well dilated by means of continued dilatation subsequent to injury or urethrorrhaphy, it frequently continues to maintain a proper caliber.

B) Patients who were not dilated or had only a few dilatations. There were 5 in our series. In 3 of these 5, surprisingly, the urethra was readily dilated. We wish to point out that all these cases involved only minor injuries with some urethrorrhaphy and with spontaneous micturition. Four patients refused any further dilatation.

C) Internal urethrotomy was done on 7 patients. This method is usually not applicable to stenoses subsequent to trauma (Marion) for the cicatrix is periurethral and not endourethral. It is indicated only in cases of incomplete ruptures of the urethra where improper treatment leads to some degree of urethral obstruction. These patients had not had urethral dilatations. Internal urethrotomy was done on 7 and we felt it was indicated in 4 of these 7; in the 3 others in whom the internal urethrotomy was done, the patients refused any other type of treatment.

D) External urethrotomy was done in 4 cases, i.e., in 3 cases as the only treatment and in 1 case after unsuccessful urethrorrhaphy done several years earlier. The results of the operation are generally not satisfactory as it fails to remove entirely the periurethral cicatrix and thus may lead to additional stenosis. It was done in cases where the condition of the patient was poor, older people with systemic disturbances in whom we did not venture to do a complete operation.

E) Cystostomy, retrograde catheterization and indwelling catheter were used in 10 cases. When the patient is seen shortly after injury with retention, cystostomy and evacuation of the hematoma are performed. Retrograde catheterization is then possible and a catheter is then passed either antegrade or retrograde at the time of cystotomy.

F) Excision of periurethral cicatrix with no urethral manipulation was done in 4 cases. This method is recommended where the cicatrization is periurethral and is compressing the urethra like a hoop and the normal structure of the urethra is fairly well preserved. By removing the cicatrix, which causes strangulation of the urethra, the latter is freed and resumes its normal appearance. This easy method can be employed in selected cases for the catheter can then be passed as a result of the urethra having been made free of the cicatrix. The results are perfect.

G) Incision of the urethral bride is applicable as an exception and was done by us in a single case, where the rupture of the urethra was caused by traction of penis in erection.

H) Partial urethrorrhaphy was done in 1 case only. This method was recommended by older urologists. In fact, the indications for this procedure are few and the method is contingent on preservation of a part of the circumference of urethra at the location of the stricture. However, this part need not be conserved. It is much better instead to make a ring-like excision of the whole circumference of the urethra and then a circular suture of both ends.

I) Complete urethrorrhaphy has been done in 30 cases. Its technique is a classic one and is well known. It may be done with precision on anterior urethra only. In ruptures of the urethra it can always be done since the defect subsequent to excision never proves to be longer than 2 or 3 cm. and this defect may be overcome by sufficient mobilization, especially of distal end of urethra. This is, in reality, the optional method for repair of the urethra in major ruptures or for late strictures.

J) Incomplete urethrorrhaphy was done in 28 cases. This method is applicable in cases where we cannot do complete urethrorrhaphy. It is applicable in ruptures of the membraneous and membranous prostatic urethra for it is here impossible to thoroughly mobilize the proximal end of the urethra. The distal end is, therefore, brought close to the posterior urethra by means of adaptation sutures, the cut ends of the urethra, however, hardly permitting an entirely good and correct adaptation of the two ends. An indwelling catheter is necessary for the purpose of keeping the ends of the urethra close together. The catheter is changed by means of the conductive thread. The results are good, however, but not so good as complete urethrorrhaphy. Suppuration about the urethra or chronic osteomyelitis, as a result of fracture of pubic bones, interferes with union and healing. This interferes with the normal postoperative healing and results in subsequent suppurations, fistulas and strictures. Urethral manipulations are sometimes also handicapped by a large dislocation of fragments of the broken bone. This occurred in 2 of our cases. In one of them we had to make a cuneiform excision of the bone so as to open the way for the urethra which had been barred by a fragment. One of our patients died on the second day after injury of myocarditis and bronchial pneumonia. No operation had been done.

SURVEY OF THE RESULTS OF TREATMENT

Of 145 cases treated (apart from one death and 4 not treated) examinations of control have been undertaken. In 118 cases it was possible to follow the patients. In 77 cases treated or not operated on, the patients could not be followed. The results are classified as very good, good, fair, and unsatisfactory. Our results were as follows:

Dilatation of urethra: Treated, 50; controlled and followed, 35. Result: very good, 30; good, 5.

Nontreated or treated by a few dilations, 5; controlled, 3. Result: good in 3 cases.

Internal urethrotomy: Treated, 7. Result: very good, 4; good, 3.

External urethrotomy in 3 cases as the only treatment (plus 1 case after urethrorrhaphy). Result: very good, 1; good, 1.

Cystostomy, retrograde catheterization and indwelling catheter: Treated, 10. Result: very good, 6; good, 3; unsatisfactory, 1.

Tunnelization of urethra: Treated, 6. Result: very good, 5; good, 1.

Excision of periurethral cicatrix: Treated, 4. Result: very good, 3; good, 1.

Incision of bride: Treated, 1. Result: very good, 1.

Partial urethrorrhaphy: Treated, 1. Result: good, 1.

Complete urethrorrhaphy: Treated, 30. Result: very good, 23; good, 3; unsatisfactory, 1; uncontrolled, 3.

Incomplete urethrorrhaphy: Treated, 28. Result: very good, 14; good, 4; unsatisfactory, 1; uncontrolled, 9.

Nontreated (declined treatment in general), 4.

Mortality due to injury, 1 (0, 66 per cent). Mortality due to operation, 0. Late mortality (after 2 years) incidental to trauma (?), 1 (0, 66 per cent).

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The Journal of Urology
Vol 75 No 1 January 1956
Printed in U S A

DILUTIONAL HYPONATREMIC SHOCK ANOTHER CONCEPT OF THE TRANSURETHRAL PROSTATIC RESECTION REACTION

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Near the end of or immediately following a transurethral prostatic resection observers infrequently note a reaction which is characterized by increasing apprehension, an elevation in blood pressure, a slow pulse, tenseness, irritability, twitching, nausea and vomiting, irrationality, confusion, shortness of breath, cyanosis, convulsion, and coma Oliguria or anuria may follow, ultimately resulting in death or spontaneous diuresis and recovery Some features of the reaction closely resemble the syndrome described by Moyer and Chassin of acute water surplus with increased intracranial pressure

Twenty-five cases are herein reported in which an attempt is made to correlate these signs and symptoms with certain changes also occurring in blood and electrolyte patterns

Bosch has shown that aged patients generally have blood volume deficiencies Many patients with obstructive prostatism have extracellular fluid deficits when examined preoperatively There is evidence that patients accumulate relatively large quantities of irrigating fluid during transurethral prostatic surgery

In those patients who have transurethral resection reactions acute relative water intoxication probably develops and unless promptly treated, a critical dilutional hyponatremia may ensue which precipitates peripheral vascular collapse Shock is known to decrease renal function and is probably a principal factor in the development of renal ischemia, insufficiency, and "lower nephron nephrosis"

DISCUSSION OF OLDER CONCEPTS OF THE TRANSURETHRAL RESECTION REACTION

Many of the early transurethral resection reactions were interpreted as acute cerebrovascular accidents, myocardial infarctions, and pulmonary infarctions Apprehension, preoperative medication, anesthesia, and blood loss shock are a few of many postulated etiological factors previously blamed for the reaction

Since 1946 and Creevy's classic articles on the subject, the literature has been replete with controversial discussions of the effect of hemolysis on the development of oliguria and anuria following transurethral prostatectomy It is very difficult to produce anuria experimentally in animals by the lysis of blood cells in the absence of shock and dehydration Hemolysis does occur during resection with water Extremely high levels of free hemoglobin are required to injure normal kidneys Twenty five hundred milligrams per cent has been suggested as a minimum concentration of hemoglobin for the onset of severe renal damage

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Read at annual meeting American Urological Association Los Angeles Calif May 16-19 1955

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It is doubtful that free hemoglobin ever reaches this level in resections. The induction of human renal failure cannot be related solely to blood hemoglobin levels during hemolysis. Considerable amounts of human hemoglobin may be injected intravenously in man without producing ill effects or significant impairment of renal function. Patients can receive considerable distilled water intravenously without permanent ill effects.

Ebert attributed the reaction to extravasation and the entrance of distilled water into the retroperitoneal space. Griffin, however, concluded in his one case of anuria and death following resection that the course was postoperative shock resulting in renal ischemia. Woodruff's reaction cases had a postoperative drop in systolic blood pressure averaging 50 millimeters of mercury lasting from one to several hours. Most case presentations in the literature had similar histories of excessive bleeding and elevation in blood pressure followed by varying degrees of hypotension, hemoglobinemia, cyanosis, oliguria, anuria, and death.

In the absence of prolonged shock and pre-existing kidney damage, there exists no satisfactory explanation for the underlying factor in the production of acute renal insufficiency and death following transurethral prostatectomy.

PATHOGENESIS OF RENAL FAILURE

The reduction of renal blood flow is of primary importance in the pathogenesis of acute renal failure. Opinions vary as to how this local ischemia is produced, and how it brings about renal failure.

Several mechanisms have been suggested by which reduction in renal blood flow and in renal filtration occurs in shock. It should be emphasized, however, that experimental shock has produced renal failure only in conjunction with renal artery constriction. Such experiments do not offer a reasonable explanation for renal failure in man, since they induce a degree of renal anoxia which would be incompatible with life.

Since the pathogenesis of the lesions of acute nephrosis remains obscure, as yet there can be no entirely satisfactory explanation for the mechanism of oliguria and anuria. Suggested theories favor an intrarenal cause, such as obstruction of tubules by casts, intrarenal compression by edema, reduction in renal blood flow, and back diffusion of filtrate through damaged renal epithelium.

Waugh states that acute renal failure may be reached by a variety of clinical pathways. He states that renal failure associated with blood destruction seems generally to occur in cases where hemolysis is both acute and massive, as in blackwater fever and incompatible transfusion. He concludes from his survey that blood and tissue pigments have little damaging effect upon the kidneys, but that together with hypotension (and, by inference, lowered filtration rate), dehydration (and possible electrolyte disturbance), or simultaneous renal damage from some other cause, they may in some way induce renal failure. In seeking a common denominator which would apply to all the various factors contributing to acute renal failure, excluding the pre- and post-renal causes, MacLean concludes that anoxia would appear to offer the most likely explanation.

Wardill found "transfusion kidneys" at autopsy in a patient who died after transurethral resection, although the patient had received no transfusion. Wardill concluded that the pathogenesis of anuria following prostatic operation was identical with that following the crush syndrome or the transfusion of incompatible blood.

The microscopic pathology of the lesion described by both Lucké and Oliver of "lower nephron nephrosis" is an accepted histopathological picture, regardless of the mechanism leading to acute intrinsic renal failure. This lesion is characterized by edema of the cells of the convoluted tubules, followed by degeneration and necrosis, with numerous heme casts, and disintegration of the continuity of the tubular membrane.

DISCUSSION OF EXTRACELLULAR FLUID AND ELECTROLYTES

The experimental use of sodium thiocyanate, radioactive sodium, and heavy water has actually added very little to the older literature on the distribution of body water into compartments in man. For practical purposes most authors consider the extracellular fluid as 20 per cent of the body weight. Five per cent is plasma and 15 per cent is interstitial fluid. This is the 1:3 ratio of plasma volume to interstitial fluid volume, as suggested by Gamble in his calculation of fluid therapy. Fluctuations in the total quantity and distribution of the extracellular fluid maintain plasma volume through a reciprocal balance of the filtration forces mediated by the osmotic pressure of the plasma proteins and the tissue tension.

Elkington found in dogs that the volume of fluid in the body and its various compartments and also the concentration of electrolytes present largely determine whether salt depletion shock occurs. Salt depletion in untraumatized animals produces a form of peripheral vascular collapse closely resembling that seen in traumatic shock: plasma volume, cardiac output, circulation rate, blood pressure, and plasma protein all decline sharply. There is a decrease only in the extracellular water and plasma water (no depletion in the intracellular water), even in profound shock. Body fluids are hypotonic in the salt-depleted dog. Hypotonicity can be caused by dilution as well as by salt loss in excess of water, and the problem becomes even more complicated when both depletion and dilution are present in the same subject. Whether the hypotonicity is the result of depletion or dilution, patients should receive treatment which restores concentration to normal; withholding salt in such patients because of fear of augmenting edema or inducing congestive heart failure may prove to be a serious error. Randall states that shock is likely when the serum sodium falls below 120 mEq/L. Much depends on the rate of fall, and he states that when the fall is rapid, shock is more likely than when it is slow.

Winkler obtained a synergistic effect by using colloid (gelatin or plasma) along with 5 per cent saline, which more rapidly restored blood pressure and blood volume.

REVIEW OF STUDIES ON IRRIGATING FLUID ABSORPTION

Evidence has accumulated in the literature that the irrigating fluids used in transurethral resections, along with any accompanying diffusable substances, enter the vascular system in significant amounts.

Creevy has demonstrated that in resection with water the free hemoglobin in plasma postoperatively averaged fifteen times the preoperative level. In other series the postoperative level exceeded the preoperative level from 25 to 56 per cent.

Jessop and Love have concluded that the rise in blood sugar occurring during transurethral resection using glucose in distilled water was proportionate to the irrigating pressure.

Bulkley has shown that the postoperative urinary output during the first 48 hours frequently exceeds the fluid intake.

The earliest recorded quantitative estimate of the amount of fluid absorbed is that of Landsteiner and Finch who "tagged" the irrigating solution with salicylic acid and found, by postoperative blood levels, that about one liter of fluid had entered the vascular system.

Hagstrom, in his studies on fluid absorption, correlated resection time with weight gain (fluid absorption) and found that from 10 to 30 cc of fluid are absorbed for each one minute of resecting time.

CANDIDATES FOR THE TRANSURETHRAL RESECTION REACTION

As we believe the reaction is caused by an acute dilutional hyponatremia, any patient is a possible candidate; however, certain predisposing conditions should be emphasized. In each, there is a notable deficit of extracellular fluid volume with a concomitant electrolyte deficiency (isotonic dehydration). See figure 1.

Cardiac disease. Many patients referred to the urologist for resection have been treated by the internist with low salt diet, digitalis, diuretics, and reduced exercise.

Hydronephrosis. The hydronephrotic kidney is a salt-losing kidney.

Salt-losing nephritis. Many patients with chronic glomerulonephritis, pyelonephritis, and nephrosclerosis are apparently unable to retain salt.

Complete urinary retention. Large amounts of sodium and chloride are usually excreted during the diuretic phase following relief of prostatic obstruction with catheter drainage.

Chronic illness, malnutrition, debilitation, and emaciation. Patients with these conditions have markedly reduced total body water, electrolytes, and blood volume.

Age. The older the patient, the greater generally is the basic deficiency. Bosch has shown the blood volume deficit to average slightly over a liter.

In the aforementioned conditions, the fluid, electrolyte, and blood reserve are minimal. It is easy to understand how patients are unable to withstand sudden large changes in their fluid compartments. Clinically, patients with isotonic dehydration have weakness, apathy, stupor, anorexia, hypoactive bowel sounds, poor skin-and-muscle turgor, wrinkled tongue, and subnormal temperature (fig. 1).

SIGNS AND SYMPTOMS OF THE REACTION

Early. Near the end of the resection the anesthetist usually notices that the patient has had an elevation in blood pressure without an increase in the pulse

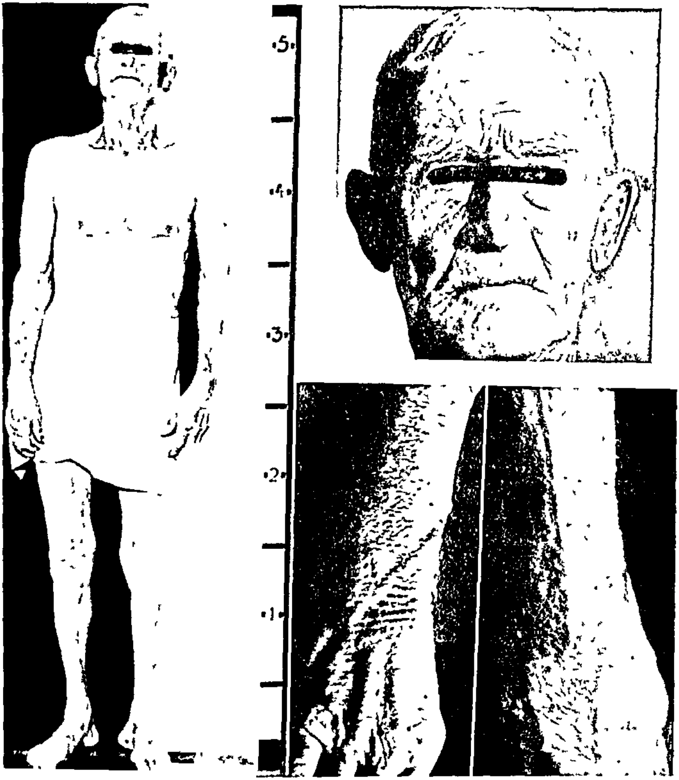

Fig 1. Isotonic dehydration

iate. He asks whether he should further sedate the patient or supplement the anesthetic agent, because of the concomitant restlessness and tenseness of the patient, doubtfully due to pain. The patient is ill at ease and slightly irrational, moves about on the table, often becomes nauseated, and vomits. The resectionist *suddenly finds moderate to marked bleeding from multiple points in the capsule,* all venous in nature.

Later. The patient may become more apprehensive, disoriented, and restless; may develop varying degrees of cyanosis, seem breathless, and complain of chest pain. Simultaneously the patient is quite tense and the blood pressure is still up 20 to 50 points, although the pulse is normal. The patient may have tetanic-like twitchings simulating convulsions, and may become semiconscious *or comatose. The wash water remains red even after repeated washings.*

Late. The patient suddenly becomes hypotensive. The cyanosis persists, oliguria is noted, and only blood passes per catheter. Signs of peripheral vascular collapse are present; often the blood pressure is unobtainable, although the patient does not look moribund.

End results. The patient may remain in coma. Despite vigorous treatment, shock may persist and the patient may develop oliguria, and then anuria; finally the patient dies from renal failure ten to twelve days later. Spontaneous recovery may occur after the oliguric period.

MATERIALS AND METHODS

The cases of 25 consecutive patients who had transurethral prostatectomy are herein reported. Fifty per cent gave a history of cerebrovascular, cardiac, or hypertensive disease. The weight of the patients 2 years prior to resection averaged 23 pounds more than at the time of resection. Ninety-two per cent manifested some degree of dehydration. All patients had stabilized blood urea nitrogen. The youngest patient was 53, the oldest was 103. Eighteen resections (72 per cent) were for benign hyperplasia, seven were for carcinoma (28 per cent). Anesthesia was low spinal (saddle). Glycine 1.1 per cent was the irrigating fluid in all cases, from a mean level approximately three feet above the hips of the patient. Samples of blood were drawn prior to and immediately after surgery, then from 48 to 96 hours postoperatively. There was no hemolysis. Cation determinations were done by the flame photometer. The amount of tissue removed was: largest, 75 gm.; smallest, 4 gm.; average, 23 gm. Resection times were: longest, 83 minutes, shortest, 30 minutes; average, 48 minutes. The standard 28 Nesbit resectoscope was used exclusively.

CASE REPORT

E. A., case No. Y-29,248, a 64-year-old white man, was first seen in the emergency room of Jefferson Davis Hospital in complete urinary retention on October 12, 1954. An indwelling Foley catheter was introduced without difficulty and 650 cc of grossly clear urine were removed. Rectal examination revealed a grade 1 benign prostatic hypertrophy. Urinalysis revealed a specific gravity of 1.010, negative albumin and sugar, and the presence of 4–6 white blood cells per low powered field. Hemoglobin was 12.5 gm. per cent, and hematocrit was 38 volumes per cent. The patient gave a history of progressive obstructive prostatism with stranguria, urgency and frequency, and nocturia 10 times. He had had an elevated blood pressure for several years treated symptomatically, but never any signs or symptoms of cardiac decompensation or cerebrovascular accident. His usual middle-age weight was 135 pounds, but over the past 3 years he had progressively lost down to his present weight of 110 pounds.

Examination revealed a blood pressure of 160/84, pulse 80, respiration 18 and temperature of 98.6. His chest was essentially clear to auscultation and percussion. He had no cardiac enlargement or murmurs, and had a regular sinus rhythm. There was grade 3 peripheral arteriosclerosis, and an estimated 4 per cent dehydration. The blood urea nitrogen was 19 mg. per cent, CO_2 combining power 23.8 mEq/L, chloride 99 mEq/L, sodium 135 mEq/L, and potassium

3.8 mEq/L. Excretory urograms were normal. Cystourethroscopic examination revealed a 1½ times elongated prostatic urethra. The lateral lobes touched in the supramontane urethra for approximately one centimeter.

On October 26, 1954, under low spinal anesthesia, a transurethral resection was accomplished in approximately 55 minutes, removing 32 gm. tissue. At the end of the resection the operator noticed that the bleeding was profuse. Many open venous sinuses were seen. The anesthetist noted a progressive elevation of blood pressure to 200/100 and increasing apprehension. Concomitantly, the patient complained of restlessness, became nauseated, and suddenly stated that he was going blind. He vomited and became quite tense and mildly cyanotic. The resectionist continued futilely to attempt fulguration, prolonging the operation an additional 28 minutes, finally stopping, stating that he had fulgurated all the arterial bleeders but could do nothing with the venous bleeding. The blood pressure began to fall and in 40 minutes was down to 80/40 with signs and symptoms of peripheral vascular collapse. Blood was administered, blood for laboratory determinations was drawn, and a second intravenous infusion of two ampules of levophed in 500 cc of isotonic saline was begun in the opposite arm to stabilize the blood pressure at 120/80. Awaiting the serum sodium level the following were computed:

Calculations:

Body weight = 110 lbs. (50 kg), ECF = 20% BW, Pre-op Na = 135 mEq/L. Clinically pt. 4% dehydrated, so ECF = 16% BW or 8 kg. (liters)

Total resection time 83 min.; fluid absorbed 20 cc/min (average figure from Hagstrom's studies), so 83 × 20 = 1700 cc absorbed (FA)

ECF × Pre-op Na = ECF + FA × X (where X is the post-op Na)

Substituting:

8 × 135 = 8 + 1.7 × X, X = 111 mEq/L Na

140 (normal serum Na) − 111 (post-op Na) = 29 mEq/L Na deficit

29 × 9.7 (post-op ECF Volume) = 281 mEq/L total Na deficit

1 gm. Na = 17 mEq/L, so 281 ÷ 17 = 16.5 gm. Na deficit

20 cc of 5% saline = 1 gm. of Na, so 16.5 × 20 = 330 cc of 5% saline necessary to restore ECF to isotonicity

The patient received 330 cc of 5 per cent saline over the next 90 minutes. Levophed was continued for approximately 2 hours to maintain his blood pressure around 120/80. The emergency serum sodium was reported as 114 mEq/L.

Approximately 6 hours after the termination of the resection, the patient had regained his sense of well being, tolerated oral fluids, and was excreting urine, grossly bloody. The next morning he was eating and was ambulatory. He received 500 cc of blood on postoperative days 1 and 2; postoperative chemistry determinations on day 3 revealed a hemoglobin of 10.1 gm., hematocrit of 35, serum sodium 132 mEq/L, blood urea nitrogen 22 mg. per cent, and potassium 4.1 mEq/L. He was discharged on November 7, 1954, asymptomatic.

RESULTS

Figure 2, *A* demonstrates that there is a very significant dilution of the sodium chloride ions in the patient who had a reaction. It also shows a considerable

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The Journal of Urology
Vol 75 No 1 January 1956
Printed in U S A

RADICAL RETROPUBIC PROSTATECTOMY FOR CARCINOMA

LYTLE ATHERTON AND L DOUGLAS ATHERTON

Inasmuch as radical retropubic prostatectomy has gained notoriety recently, we thought that it would be interesting to report our immediate results in 51 such operations performed during the past 6 years

Prostatic carcinoma is unique because it usually occurs in an older age group, and many of the patients are already beset by a degenerative disease which may cause death within a very few years Moreover, we have at hand powerful palliative measures, involving little or no risk to the patient, which are likely to keep carcinoma under control and allow him a comfortable existence for an average of two or three years These two factors alone complicate our judgment and perhaps call for conservatism, whereas carcinoma in other localities and in different age groups has encouraged radical surgery To balance this picture, all physicians have seen the lingering misery caused by unalterable skeletal metastases

The extremes of this disease have been clearly defined and the treatment agreed upon The one extreme is the small, localized nodule of carcinoma confined to the limits of the prostate in a patient without evidence of metastasis and who is found to be a good operative risk with a reasonable life expectancy The second extreme is the inoperable, extensive carcinoma presenting some degree of fixation and invasion into seminal vesicles and bladder floor, with or without evidence of distant spread Here, the problem of proper therapy is simple

However, in a number of patients the disease presents itself between these two extremes, either in extent of local disease, or in the prediction of longevity We might facetiously call these "nearly inoperable," or perhaps "almost operable" It is our belief at the present time that the radical retropubic operation is an instrument better qualified as curative in this relatively large in between group

At the present time, our judgment having been mellowed by a fair amount of experience with both retropubic and perineal methods of prostatic surgery, we very definitely favor radical perineal prostatectomy for the classical small prostate with an early carcinoma This operation, in our experience, is less sanguinous, is blessed with a more comfortable postoperative course, has comparable functional results, and has the distinction of a good cancer operation We favor the retropubic route in cases of carcinoma associated with a considerable amount of benign hypertrophy, or in those cases where the extent of the carcinoma is greater than optimum and yet clinically confined to the prostate and proximal seminal vesicles We agree that tumor cells found in the tissue about the seminal vesicles are extremely unfavorable prognostic signs However, in the light of our present knowledge, it is not certain proof that the disease is beyond surgical cure

Read at annual meeting Southeastern Section of American Urological Association, New Orleans, La March 20 24, 1955

In dealing with large prostates involved in carcinoma, one finds by the perineal route that the prostate fills the incision like a cork in a bottle, and the gland either has to be fragmented or else its appendages must be taken by something less than thorough and accurate dissection. Retropubically, large prostates with the attached seminal vesicles and generous tissue about them, along with the bladder neck, can be removed in one piece with good visualization and ample opportunity for careful dissection. In cases so elected for retropubic surgery in which the examiner is not certain of the presence of carcinoma, we favor perineal biopsy and frozen section, followed by the radical operation if the diagnosis is confirmed. We favor this in a single stage procedure. If, while in the perineum, the prostate is freed extracapsularly and the urethra cut through, the retropubic phase is facilitated.

One of the points Dr. Richard Chute made in so graphically and splendidly presenting this subject last year was that the retropubic approach, by reason of being more familiar to a sizable portion of our fraternity, might result in a greater number of attempted operative cures for this disease.

The technique of the radical retropubic operation is fairly straight-forward. When we first began doing the procedure the latter part of 1948, the problem of anastomosing the reconstructed bladder neck to the membranous urethra quickly became a challenge. The problem was solved simply by threading two long sutures on either side of the reconstructed bladder neck through to the perineum on respective sides of the membranous urethra and tying them over a gauze sponge (figs. 1 and 2).

By way of commenting on the anastomosis and precautions recommended in preserving continence, we suggest that the stay-sutures be placed approximately 1 cm. lateral to the membranous urethra on each side, and that they

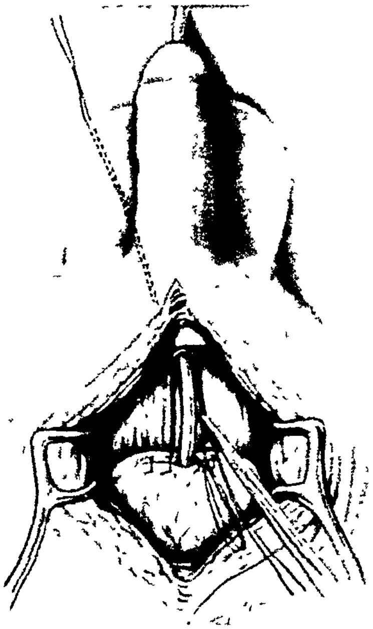

FIG. 1. Placing anastomotic stay sutures

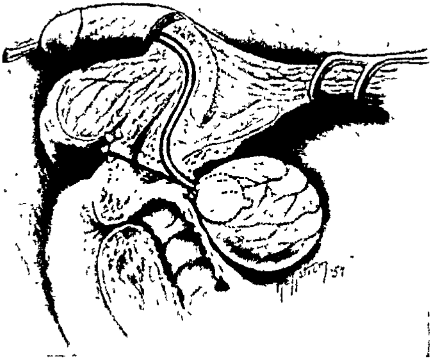

FIG. 2. Anastomosis completed

be tied with minimal tension so that there will be little risk of ischemic necrosis of the structures lying between bladder and perineum. Occasionally when a large prostate has been removed one finds that the reconstructed bladder neck will not quite reach the membranous urethra, and we believe that little is to be gained by tying these stay-sutures so tightly that a deep depression results in the perineum beneath the gauze sponge. Dr. Chute has advanced a modification in reconstructing the bladder neck to bridge any gap without tension.

The following statistics concern only the immediate results in 51 radical retropubic operations. Our operative mortality has been zero. Three patients have died in the hospital (5.9 per cent). Two of these deaths were due to pulmonary embolism, one from miliary tuberculosis. The latter case will be mentioned again.

In one case a stricture developed at the vesical neck. The patient was later subjected to transurethral resection of the stricture and a focus of carcinoma was found in the tissue removed.

Osteitis pubis developed in one patient.

In 41 patients urinary control was complete and quite satisfactory to both patient and doctor within one day to six months. On the average it returned within one week. Of the 10 cases without satisfactory control, three included the hospital deaths in which no evaluation of control was possible. Two patients died within 3 months; one had some degree of incontinence and the other was unable to empty his bladder without help, possibly due to the removal of most of the trigone at time of operation. In retrospect, both of these should be classified as "nearly operable." Two patients have poor control and wear Cunningham clamps. Both can stay dry in bed, and both can stop and start on demand. One patient has mild stress incontinence. One patient was not followed beyond his hospital stay. One patient, with proven recurrence in the region of the anastomosis, has intermittent control depending on the status of his vesical neck stricture.

Of the 51 cases operated on by radical retropubic prostatectomy, not all were done for carcinoma. In 40 cases carcinoma was suspected. In 2 cases carcinoma was unsuspected and found. In 28 cases carcinoma was suspected and found. In 11 cases the operation was performed either for recalcitrant prostatitis or early in the series when we were quite enthusiastic about the operation and were considering it a worthy prophylactic measure in patients who were beyond sexual interest and who were good operative risks.

The preoperative evaluation was made in all but 2 cases by rectal palpation alone. In one of the 2 cases, carcinoma was found in the tissue removed by transurethral resection; in the other, the diagnosis was made at operation by frozen section when we unsuspectingly ran into a firm prostatic mass at the time of a proposed simple retropubic prostatectomy for what clinically appeared to be a large benign gland. Frozen section was taken from the anterior surface of the gland and was reported as a rather anaplastic epidermoid carcinoma.

In general we have attempted to classify the preoperative clinical impression on a basis of definite carcinoma, some cases of which were of the "almost inoperable" or "nearly operable" variety (3 plus); most likely carcinoma (2 plus); and possibly carcinoma (1 plus). One of the 2 plus cases was the patient who had unsuspected tuberculous prostatitis (an elderly man with about 500 cc residual urine) a normal excretory urogram, a negative x-ray of the chest, and a prostate that felt suspiciously like diffuse carcinoma. He died a week later with mysterious toxic manifestations which we attributed in retrospect to miliary tuberculosis. This was the only case done in a small hospital in which the report on the specimen was not available for about 10 days.

The rather significant error in diagnosis in the group of carcinoma suspects is extremely good evidence in favor of preliminary confirmation by biopsy if sexual impotence or an occasional case of needless incontinence is to be avoided. Most of us are now agreed that perineal biopsy is the most reliable tool for this purpose. On the other hand, one case of totally unsuspected carcinoma was found, not including the two diagnosed by frozen section and by transurethral resection. These three would not have been tagged for perineal biopsy in any event. This is a thought-provoking problem to which there is no factual answer. The individual solution lies in one's own philosophy and experience.

It is with great reluctance that we present any statistics relating to longevity

TABLE 1. *Longevity*

Alive and free of disease	12 (22-65 mos.)
Free of disease 2 yrs. and lost to followup	1
Not followed for some reason	3
Living with carcinoma	6
Died of prostatic carcinoma	4
Died of other disease without ca. prostate	2
Died of other disease with ca. prostate	0
Hospital mortality	2
	30

simply because there are neither enough cases to be very sound statistically, nor has the followup been sufficient to draw any very promising conclusions. The data are given in table 1.

As a general measure, those patients with a small area of carcinoma, proven to be small by examination of the specimen and well confined within the substance of the prostate, are not given palliative hormones. Patients who have fairly extensive carcinoma diffusely involving the prostate, with or without involvement of the vesicles, are routinely kept on stilbestrol. If or when metastasis or local recurrence appears, we usually then perform orchiectomy. Some of the patients in this series have been on stilbestrol constantly, and one has every right to assume that that their continued benign appearance may be related to the hormones. That is one sincere criticism to presenting figures at such a time.

SUMMARY

The indications for use of radical retropubic prostatectomy for carcinoma have been cited. The immediate results following 51 radical retropubic prostatectomies using the type of vesicourethral anastomosis illustrated are outlined.

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The Journal of Urology
Vol. 75, No. 1, January 1956
Printed in U.S.A.

PROSTATIC ENZYMES AND ABNORMAL BLEEDING

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Our knowledge of the enzymes of the body has increased considerably in recent years with the result that their role in health and disease has become increasingly apparent.[1] The proteolytic enzymes of the plasma have been studied and have been incriminated in certain cases of abnormal bleeding.[2, 3] That the prostate contains a proteolytic enzyme has been known for some time,[4] but the clinical significance of this enzyme as a cause of abnormal bleeding has only recently been emphasized. The purpose of this report is to call attention to the prostatic proteolytic enzyme and to emphasize its possible clinical importance.

A review of the current concept of the proteolytic enzyme system of the plasma is necessary and can best be illustrated by a simple diagram (fig. 1). In general, there is a dynamic equilibrium between an active enzyme called plasmin and its inhibitor called antiplasmin. The precursor of plasmin is termed plasminogen. Plasmin is capable of digesting many of the blood coagulation factors as well as the end product of coagulation, fibrin. Thus it is evident that it is proteolytic rather than just fibrinolytic. For this reason, conditions in which there is an excess of plasmin may be characterized by abnormally low concentrations of prothrombin and fibrinogen as well as instability of the blood clot from lysis of fibrin.

MacFarlane and Biggs,[2] and Biggs, MacFarlane, and Pilling[5] have demonstrated increased plasmin activity in humans after fear, exercise, trauma, and parenteral administration of adrenalin. Approximately one-half of the preoperative and postoperative patients studied showed some evidence of abnormal plasma proteolytic activity, regardless of the type of surgical procedure. The studies of these investigators and others have resulted in the generally accepted opinion that the alarm reaction is the basic mechanism for abnormal plasma proteolytic activity. However, the exact details of the mechanism are at present undetermined.

The means by which plasminogen is activated is still unexplained, but there is evidence to indicate that tissue cells contain an enzyme activator which on release into the plasma causes the conversion of plasminogen to plasmin. Mathey, et al.[6] have demonstrated abnormal proteolytic activity in the blood of the pulmonary vein before its appearance in the arterial blood and are of the opinion

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Read at annual meeting, Southeastern Section of American Urological Association, New Orleans, La. March 20–24, 1955.

[1] Tagnon, H. J.: Enzymes in clinical medicine. New Eng. J. Med., **249**: 650, 1953.

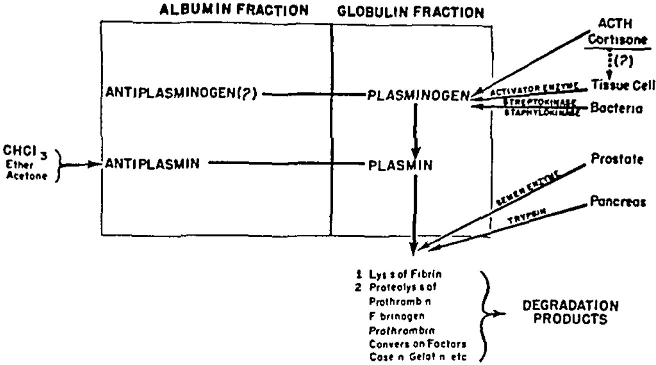
[2] MacFarlane, R. G. and Biggs, R.: Fibrinolysis. Its mechanism and significance. Blood, **3**: 1167, 1948.

[3] Scott, E. V. Z., Matthews, W. F., Butterworth, C. E. and Frommeyer, W. B.: Abnormal plasma proteolytic activity. Diagnosis and treatment. Surg., Gynec. & Obst., **99**: 679, 1954.

[4] Huggins, C. and Neal, W.: Coagulation and liquefaction of semen. J. Exp. Med., **76**: 527, 1942.

[5] Biggs, R., MacFarlane, R. G. and Pilling, J.: Observations on fibrinolysin. Experimental activity induced by exercise or adrenaline. Lancet, **1**: 402, 1947.

[6] Mathey, J. J., Doumet, P., Soulier, J. P., LeBallogh, A. G. and Fayet, H.: Hemorrhagies graves au cours d'interventions thoraciques par incoagulabilite sanguine due a la fibrinolyse. Mem. Acad. de Chir., **16**: 977, 1947.



SCHEMA OF PLASMA PROTEOLYTIC ENZYMES AND PROPOSED MECHANISM OF ACTION OF VARIOUS COMPOUNDS, BACTERIA AND TISSUE PRODUCTS

FIG 1

that lung tissue is particularly capable of causing activation of plasminogen However, Tagnon and Petermann,[7] Astrup and Permin,[8] and others have demonstrated a tissue activator enzyme in many other organs and are of the opinion that the ability to activate plasminogen is a general property of all tissue cells

Studies on human semen have revealed the presence of a proteolytic enzyme which was shown by Huggins and Neal[4] to have its origin in the prostate gland This enzyme, which is responsible for the liquefaction of semen, was found to have the same properties as the enzyme of the plasma (plasmin), but no conclusion was drawn as to its identity with plasmin Their studies were extended and clarified by Von Kaulla and Shettles[9] who found semen to contain not only an active proteolytic enzyme which was capable of dissolving a blood clot but also a proenzyme similar to plasminogen An active enzyme could be obtained by activation of this precursor with streptokinase To complete the analogy between the enzyme systems of semen and blood an antienzyme capable of neutralizing the active enzymes was also found to be present The clinical importance of the prostatic proteolytic enzyme has recently been pointed out by Tagnon[10, 11] who reported the presence of abnormal amounts of proteolytic enzyme in the blood of many patients with metastatic prostatic carcinoma Metastatic carcinoma cells were shown to be the origin of the enzyme

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[7] Tagnon, H J and Petermann, M L A proplasmin activator from mammalian tissue J Clin Invest, 28 814 1949

[8] Astrup, T and Permin, P M Fibrinolysis in the animal organism Nature, 159. 681 1947

[9] Von Kaulla K N and Shettles, L B Relationship between human seminal fluid and the [illegible] Exp Biol and Med, 83: 692, 1953

[10] [illegible] F Schulman, P and Kravitz, S C The significance of [illegible] with metastatic cancer of the prostate Cancer, 6: 63, 1953

[11] Tagnon H J, Shulman P Whitmore, W F and Leone L A Prostatic fibrinolysin Study of a case illustrating role in hemorrhagic diathesis of cancer of the prostate Am J Med 15 875 1953

The following case report illustrates the problems encountered when an increased amount of circulating proteolytic enzyme is present in a patient with disseminated prostatic carcinoma.

CASE REPORT

A 53-year-old white man was first seen on May 5, 1953 complaining of generalized skeletal pain of 16 months' duration, accompanied by a weight loss of 40 pounds. Because of obstructive urinary symptoms he had consulted a urologist who made a diagnosis of carcinoma of the prostate. Treatment with oral estrogens had been started but, because of only temporary and slight alleviation of pain, the patient had discontinued estrogens. Two weeks previously he had vomited blood on two occasions, and one week previously he had noticed ecchymotic areas on the tibial aspects of both legs.

Physical examination revealed a pale, chronically ill, white man. The examination was otherwise essentially negative except for rectal examination which confirmed the diagnosis of prostatic carcinoma with local extension. There were also ecchymotic areas scattered over both lower extremities.

Laboratory studies showed a moderate elevation of the serum acid phosphatase and a severe normochromic anemia. Urinalysis was negative. Since the presence of ecchymoses suggested the possibility of circulating proteolytic enzyme, a specimen of blood was obtained for determination of enzyme activity. This blood clotted normally, but the clot dissolved completely within 6 hours, thereby confirming the presence of the enzyme. Roentgenologic examination revealed changes compatible with extensive metastatic carcinoma of the ribs, vertebrae, and pelvis.

Because of the extensive carcinoma with progressive discomfort from bone metastases in spite of intermittent estrogen therapy, an orchiectomy was thought advisable. Following administration of 500 cc of blood by transfusion a specimen of the patient's blood clotted normally with the clot showing only slight evidence of lysis within 24 hours. This was interpreted as evidence that the proteolytic enzyme of the plasma had been almost completely neutralized by an antienzyme in the transfused blood. After transfusion of a total of 1500 ml. of blood, a bilateral orchiectomy was done under local anesthesia with no unusual bleeding being encountered during the operation. A specimen of blood drawn immediately prior to the operation clotted normally. Several hours after the operation the scrotal swelling had progressed to alarming proportions, and at this time the clot of the blood specimen drawn prior to the operation was seen to have dissolved completely. The scrotum was reopened and approximately 1500 ml. of liquid blood were evacuated. Bulky dressings were applied to the scrotum and pressure applied by elastic bandage.

Postoperatively an attempt was made to neutralize the circulating fibrinolytic enzyme by repeated intravenous administration of blood and serum albumin. A specimen of blood was drawn every 6 hours for the first seven postoperative days with each specimen being observed for a total of 24 hours. At the time the specimens were drawn a transfusion of blood or serum albumin was given if any of the three previous specimens showed evidence of lysis of the blood clot All blood was collected in sterile tubes and kept at the patient's bedside In addition to the above treatment, 15 mg of stilbestrol were given orally beginning on the first postoperative day

The hematoma of the scrotum gradually disappeared, and the patient was discharged on the twentieth postoperative day with a draining sinus in the left scrotum He was instructed to take 5 mg of stilbestrol 3 times daily For approximately 6 months the patient remained well with few pains, but 7 months after orchiectomy he again was complaining of severe pains in the back and pelvis Eight months after operation there was no lysis of the patient's blood clot, no ecchymosis, and only slight skeletal pain

DISCUSSION

The presence of an abnormal amount of circulating proteolytic enzyme was recognized prior to operation Because transfusions given before the operation had resulted in disappearance of the fibrinolysis it was thought that the enzyme had been adequately neutralized, however, the hemorrhage which occurred after the operation showed that such was not the case, vigorous efforts being necessary to prevent exsanguination

It is interesting to note that the patient had a very satisfactory remission of symptoms with estrogen therapy following orchiectomy This was in conjunction with disappearance of the abnormal amounts of proteolytic enzyme in the blood and is in accord with the findings of Tagnon[19] who considers the remission of symptoms and disappearance of the plasma proteolytic activity to be indications of suppression of the cancer cells Whether the transfused blood and albumin or the estrogens were instrumental in bringing about the disappearance of enzyme activity is impossible to say Concentrated serum albumin was administered empirically because it is known to contain antiplasmin and is effective in conditions in which there is abnormal bleeding as the result of increased circulating plasmin[3]

Recently 2 patients have been observed who suffered abnormal bleeding following transurethral resection of the prostate gland Studies on the blood of these patients revealed evidence of a proteolytic enzyme which was responsible for abnormal bleeding as the result of destruction of coagulation factors as well as lysis of fibrin These cases are reported in detail elsewhere[3] Whether or not the increased circulating enzyme was the result of liberation into the circulation of the prostatic proteolytic enzyme is a matter of speculation

In general, persons undergoing surgery are subject to the hazards of bleeding from abnormal plasma proteolytic activity under the following circumstances 1) when there is activation of plasminogen as a result of the alarm reaction, 2) if tissue activator substances are released into the circulation resulting in the activation of plasminogen, and 3) when proteolytic enzymes from sources such as the prostate or pancreas are released into the circulation

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[19] Tagnon H J Schulman, P, Whitmore W F and Kravitz S C The hemorrhagic syndrome of metastatic prostatic cancer and its treatment J Clin Invest, **31** 666, 1952

The enzyme which has been identified in the plasma of 12 per cent of patients with metastatic carcinoma of the prostate has been termed "prostatic fibrinolysin" by Tagnon[10] and is probably the same enzyme which was studied in the semen by Huggins and Neal.[4] The fact that metastatic prostatic carcinoma cells were proven by Tagnon to contain the proteolytic enzyme makes obvious the analogy between elevations of serum acid phosphatase and elevations of the serum proteolytic enzymes in these patients. Hypoprothrombinemia, fibrinogenopenia, and lysis of fibrin, which are the results of increased amounts of the circulating enzyme, were seen to disappear following estrogen suppression of the prostatic carcinoma. Similarly these abnormalities could be brought on by androgenic stimulation of the neoplasm.

The importance of the enzyme in a patient on whom an operation is contemplated is well demonstrated by the reported case. Even though the presence of the enzyme was recognized and steps taken to neutralize it, the outcome was almost fatal because of the unexpected persistence of the enzyme in amounts sufficient to cause lysis of the blood clot. It was only after vigorous therapy with blood and serum albumin that hemostasis was maintained. The administration of estrogens after the operation undoubtedly played a part by suppressing the cancer cells, thereby preventing the continuous production of proteolytic enzyme.

If the presence of the enzyme is not recognized, or if it is not neutralized adequately, surgery is exceedingly hazardous. The most common surgical procedures on patients with metastatic prostatic carcinoma are orchiectomy and transurethral prostatic resection. Bilateral adrenalectomy has recently been advocated for this condition, but its use is certainly not common. Any patient with metastatic prostatic carcinoma who is to have a surgical procedure should be carefully studied for the presence of increased plasma proteolytic activity. A simple method of doing this is to collect a specimen of the patient's blood in a sterile test tube and allow it to clot. The clot should be observed at intervals for 24 hours and, if there is no evidence of lysis at the end of this time, the proteolytic enzyme can safely be assumed not to be present. Even partial lysis of the clot is evidence of increased plasma proteolytic activity.

TREATMENT

It is the author's firm conviction that no surgical procedure should be done on a patient who is known to have elevated plasma proteolytic activity. If such an elevation is present or even suspected, it is imperative that prophylactic treatment with estrogens be continued until the enzyme activity disappears. Because of the possibility of unrecognized plasma proteolytic activity, it is probably advisable to give estrogens to all patients with metastatic prostatic cancer before doing any operative procedure.

The albumin fraction of the serum contains the antienzyme (antiplasmin) which is known to neutralize the active proteolytic enzyme (plasmin). Under normal conditions there is equilibrium between these two, but pathological proteolysis can occur when the amount of enzyme increases or the titer of antienzyme decreases. It is not known whether the albumin fraction of the serum contains an antienzyme specific for the prostatic proteolytic enzyme In the reported case intensive treatment with blood, serum albumin, and estrogens proved effective in preventing lysis of the blood clot Serum albumin has been shown to provide sufficient antienzyme in conditions in which there is excess plasmin Therefore, until there is evidence to the contrary, it seems advisable to administer serum albumin, plasma, or whole blood to any patient who exhibits abnormal bleeding as the result of an excess of plasma proteolytic enzyme, regardless of the source of the enzyme

Stefanini and Gendel[13] extensively investigated a patient with disseminated prostatic carcinoma who experienced abnormal bleeding as the result of increased plasma proteolytic activity Administration of fresh whole blood, plasma, serum and prothrombin were ineffective in controlling the severe bleeding Following administration of cortisone, there was striking and prompt cessation of the bleeding accompanied by laboratory evidence of decreased fibrinolytic activity Solomon and Stefanini[14] reported further on the use of cortisone and corticotrophin in treating 8 patients with excessive fibrinolysis Three of these patients had disseminated prostatic carcinoma, while 2 patients had undergone prostatectomy for benign adenoma In every case there was a prompt fall in plasma proteolytic activity following administration of cortisone or corticotrophin This was thought to be due to a rise in plasma antifibrinolysin These investigators are of the opinion that corticotrophin is more effective than cortisone when used for control of the bleeding manifestations of "fibrinolytic states"

It is obvious from the foregoing discussion that the treatment of abnormal bleeding resulting from the elevated plasma proteolytic activity associated with disseminated prostatic carcinoma should have as its objective the following

1) Restoration and maintenance of blood volume

2) Neutralization of the enzyme by administration of serum albumin or plasma

3) Increasing the circulating antienzyme by administration of cortisone or corticotrophin

4) Preventing continuous production of the enzyme by estrogenic suppression of metastatic cancer cells

SUMMARY

A case is reviewed of extensive metastatic carcinoma of the prostate with abnormal post-orchiectomy bleeding as the result of a circulating proteolytic enzyme The probable origin of the enzyme is discussed

Treatment of the abnormal bleeding is discussed

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[14] Solomon, L and Stefanini, M Control of bleeding manifestations in "fibrinolytic states" by corticotropin and cortisone Clin Res Proc , 2 33, 1954

THE JOURNAL OF UROLOGY
Vol. 75, No 1, January 1956
Printed in U.S.A.

PRIMARY AMYLOIDOSIS OF THE LOWER GENITOURINARY TRACT

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Primary amyloidosis is an uncommon degenerative disease of obscure etiology. The mechanisms of formation and character of the deposits are only partially understood. In the early literature the German pathologists reported not infrequently on the subject as observed in autopsy material.[1-5] A number of clinico-pathological and experimental studies have appeared in the more recent literature and have indicated the involvement of many organ-systems usually considered free from the disease.[6-14]

Several classifications of the disease have been made from a morphological and anatomical viewpoint.[7, 9, 13, 14] King[15] classified the disease on an anatomical basis depending upon the location of the amyloid deposit. Bauer and Kuzma[8] prefer the term "paramyloid" to characterize the atypical distribution and staining reactions. Lindsay[9] and Dahlin[7] feel that when the mode of formation is established all types of amyloidosis will become secondary in classification.

Primary amyloidosis may be classified as: 1) systemic (diffuse depositions in organs involved), or 2) localized (tumefactive or diffuse depositions in the affected organ). It is distinguished from the secondary form by the absence of suppurative processes; deposition in unusual sites (trachea, larynx, heart, thyroid, skin, lungs, stomach, colon, and genitourinary tract); and irregular staining reactions.

Read at annual meeting, American Urological Association, Los Angeles, Calif., May 18, 1955.

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[8] Bauer, W. H. and Kuzma, J. F.: Solitary "tumors" of atypical amyloid (paramyloid). Am. J. Clin. Path., **19:** 1097–1112, 1949.

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[10] Letterer, E.: Some new aspects of experimental amyloidosis. J. Path. & Bact., **61:** 496–498, 1949.

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[13] Higgins, H. W. and Higgins, H. W., Jr.: Primary amyloidosis, a clinical and pathological study. Am. J. M. Sc., **220:** 610–615, 1950.

[14] Koletzky, S. and Stecher, R. M.: Primary systemic amyloidosis. Arch. Path. **27:** 267–288, 1939.

[15] King, L. S.: Atypical amyloid disease, with observations on a new silver stain for amyloid. Am. J. Path., **24:** 1095–1115, 1948.

We are presenting 3 cases which illustrate the clinical and pathological characteristics of primary amyloidosis of the lower genitourinary tract.

PRIMARY LOCALIZED (TUMEFACTIVE) AMYLOIDOSIS OF THE URINARY BLADDER

Miss C. L., No. 570967, a white woman, aged 54 years, was admitted to the Presbyterian Hospital December 8, 1954 because of painless, intermittent hematuria of 7 months' duration. Cystoscopic examination at monthly intervals following the onset revealed a lesion varying from a tiny blood streak on a small mucosal elevation to a 3 cm. blue-purple, bleeding, sessile mass. This was located in the dome of the bladder to the left of the midline. The variation in activity of the lesion seemingly corresponded to an estrus cycle, and a tentative diagnosis of vesical endometriosis was made.

The past history was irrelevant except for five previous hospital admissions for appendicitis, uterine fibromas, partial intestinal obstruction, cholelithiasis, Bartholin cyst abscess, and osteoarthritis.

Physical examination revealed no abnormal findings. The blood pressure was 128/82, and the pulse and temperature were normal. The blood count and urinalysis were normal. Excretory urograms were normal. An electrocardiogram revealed left ventricular hypertrophy, and a chest x-ray was negative.

On December 9, 1954 a segmental resection of the bladder lesion was performed revealing a 3 cm. mass in the dome of the bladder sharply elevated above the surrounding normal mucosa, well localized, purple-red in color, and hemorrhagic in character (fig. 1). The postoperative course was uneventful. The Paunz test revealed a Congo red uptake of only 21.6 per cent. The serum proteins and A/G ratio were normal. The patient was discharged on the fifteenth postoperative day and has remained asymptomatic and in perfect health.

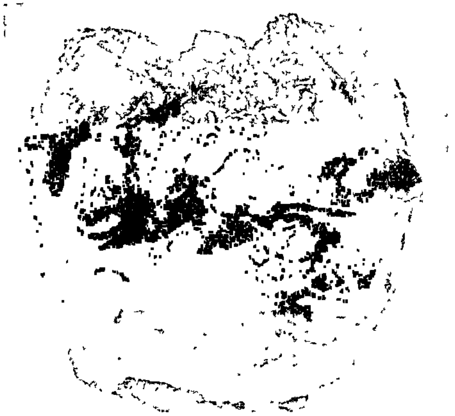
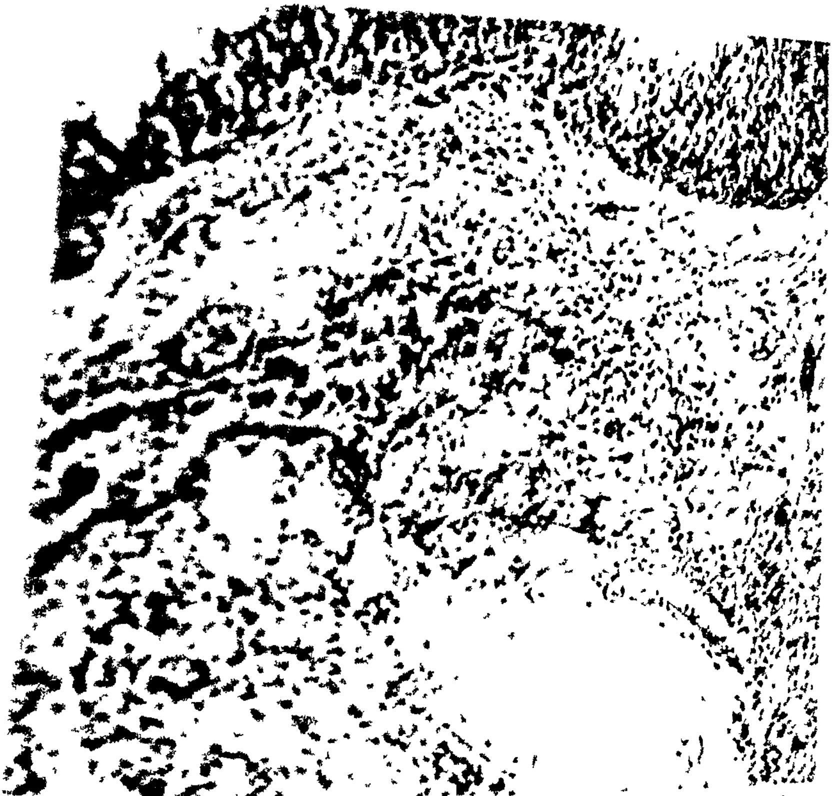


FIG. 1. C. L. Gross specimen of localized primary amyloidosis of bladder.



[illegible] shown in figure 1. Note amyloid deposits [illegible] infiltration of submucosa and [illegible]

[illegible] mass revealed large, irregular areas [illegible] ted with large, discrete, amorphous [illegible] amorphous masses were present [illegible] ar manner, occasionally obliter- [illegible] also invaded the underlying [illegible] In some instances, the connective [illegible] of round cells into the submucosa [illegible] red stains gave characteristic [illegible] Diagnosis: Primary amyloi- [illegible]

[illegible] recorded in 1897 the first de- [illegible] the urinary bladder. Lucksch [illegible] only one that had an associated [illegible] (tuberculosis) found as a causative factor in secondary amyloidosis. In a patient with primary systemic amyloidosis at autopsy, DeWolf and Clarke[16] found a large translucent deposit of amyloid beneath the vesical serosa. Involvement of the urinary bladder in primary systemic amyloidosis also has been noted by Lubarsch, Wild, Konigstein, Warren, and Hoenisch. In Hoenisch's case there was a carcinoma of the bladder. In no instance of vesical involvement, secondary to primary systemic amyloidosis, was there evidence of hematuria.

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[16] DeWolf, H. and Clarke, B. E.: Primary amyloidosis. Am. J. Clin. Path., 20: 165-170, 1950.

Ten previously reported clinical observations of primary tumefactive amyloid disease localized in the bladder have been reviewed[17-25] (table 1)

The etiology of primary localized amyloidosis is unknown Multiple myeloma is considered a common antecedent to this form of amyloid degeneration In fact, Koletzky and Stecher[14] give myeloma separate recognition in their classification of amyloidosis Rosenblum and Kirschbaum[26] do not believe that these local deposits occur without the presence of myeloma Bauer and Kuzma[8] feel there is no acceptable explanation of the pathogenesis of local amyloid formation They *propose the possibility of a local deposition caused by a derangement of protein* exchange between cell and plasma, and the appearance of abnormal proteins secondary to local inflammation or trauma

The characteristic symptom of the vesical lesion is painless gross hematuria This occurred in all clinical cases and was painless in nine of the eleven The hemorrhage into the tissues occurs from perforation of the blood vessels with the walls weakened by amyloid infiltration Mallory[27] states that 40 per cent of patients with primary systemic amyloidosis bruise easily due to amyloid infiltration of the subcutaneous vascular channels The hemorrhage also accounts for the purple-red appearance which, on resorption and later hemorrhage, may resemble endometriosis on cystoscopic examination Only Craig[21] has mentioned the need for the differential diagnosis of endometriosis in the consideration of this form of amyloid disease

There was no significant sex distribution in this group of patients, however, it *is of interest that over one half have been in the 50 to 60 age group*

The cystoscopic picture varies greatly in the several reports but generally reveals a solid, circumscribed, elevated, sessile mass with a hemorrhagic, irregular surface of yellowish tint frequently oozing blood Occasionally there is mucosal ulceration Almost invariably the mass appears as an infiltrating neoplasm In Leiter's report,[23] it appeared as an extrinsic mass pushing the vesical wall inward

The differential diagnosis of primary tumefactive amyloid deposits in the urinary bladder must include tumor, endometriosis, cavernous hemangioma, cystitis cystica and glandularis, and primary systemic amyloidosis involving the

[17] Chwalla, R A case of amyloidosis at the bladder neck resembling a tumor Urol & Cutan Rev , **36** 381–384, 1932

[18] Rusche, C F and Bacon, S K Solitary tumor like amyloidosis of the urinary bladder Tr Am A Genito Urin Surg , **34** 163 168, 1941

[19] Corbitt, R W , Broders, A C and Pool, T L Amyloidosis of the urinary bladder J Urol , **52** 153–157, 1944

[20] Purcell, H M and Brown C E Localized amyloidosis of the urinary bladder U S Nav M Bull , **46** 1607 1610, 1946

[21] Craig, L G Amyloid tumor of the bladder J Urol , **61** 365–370, 1949

[22] Senger, F L Thomley, M W and McManus, R G Primary amyloidosis of the bladder J Urol **63** 790–793, 1950

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[26] Rosenblum A H and Kirschbaum, J D Multiple myelomas with tumor like amyloidosis J A M A , **106** 988 991 1936

[27] Mallory, T B Castleman B and Parris, E E Case records of the Massachusetts General Hospital New Eng J Med , **240** 572 577, 1949

TABLE I

Author	Year	Sex	Age	Pre-existing and Associated Disease	Autopsy Findings	Symptoms	Cystoscopic Examination	Treatment
1. Solomin	1897	Female	73	Arteriosclerosis; chronic nephritis; cerebral hemorrhage	8 cm. plaque, yellow color, posterior wall of bladder	—	—	—
2. Lucksch	1904	Female	42	Tuberculosis of lung, larynx and small intestine	Multiple tumors up to 2 cm. in diameter, 0.5 cm. elevation, yellow in color	—	—	—
3. Chwalla	1932	Male	57	Papillomatous degeneration of bladder neck	—	Painless hematuria, urinary retention	Solid tumor of uneven surface at vesical orifice extending into prostatic urethra	Segmental bladder resection—dark colored, easily bleeding tumor. Curettage of urethra
4. Rusche and Bacon	1941	Female	51	Stomach ulcer	—	Painless hematuria	Infiltrating tumor of left lateral wall and dome	Segmental bladder resection; tumor 6 x 6 x 2 cm. with central ulceration. Cystoscopic exam. 9 months later negative
5. Rusche and Bacon	1941	Male	69	Early benign hyperplasia prostate	—	Hematuria, frequency, fever and chills	Localized, elevated, irregular, hemorrhagic 3 cm. area on right posterolateral wall	Transurethral fulguration. Three years later transurethral resection and fulguration, with extensive recurrence
6. Corbitt, Broders and Pool	1944	Female	59	None	—	Hematuria, dysuria	Fungiform growth from 1 cm. above left ureteral orifice, left lateral wall, dome, and portion of right lateral wall	Segmental bladder resection. Irregular elevations and convolutions indistinguishable from tumor
7. Purcell and Brown	1946	Male	34	None	—	Painless hematuria	Sessile mass, anterior-superior aspect of bladder. Yellow, edematous appearance, oozing blood	Segmental bladder resection. Mucosa soft, red and velvety over lesion; surrounding mucosa covered with yellow-white plaques
8. Craig	1949	Male	47	None	—	Massive hematuria	Slightly elevated, infiltrating, circumscribed 1 inch tumor, yellow-red in color, oozing blood	Transurethral biopsy and fulguration. No recurrence after 6 years
9 Senger, Thomley and McManus	1950	Female	49	None	—	Painless hematuria	Irregular, circumscribed, flat, reddish mass 6 x 8 cm. in diameter on floor and posterior vesical wall	Segmental bladder resection; removal ¾ tumor; radon seeds implanted in remaining ¼ of tumor. Three months later, no tumor. Bladder capacity 3 oz.

10 Leiter	1950	Female	53	None	—	Painless hematuria	1) Bleeding area apparently arising from dilated vein, posterolateral aspect of bladder 2) Four months later small area elevated reddish mucosa above right ureteral orifice 3) Nine months later localized bulging mass beneath normal mucosa, yellow tint, right side of bladder	Transurethral fulguration on four separate occasions without cure
11 Roen and Wiener	1951	Male	55	None	—	Painless hematuria	Yellow red, flat, infiltrating irregular mass region of trigone	Transurethral resection No recurrence 22 months later
12 Poutasse and Fisher	1952	Female	56	None	—	Painless hematuria	3 cm papillary lesion region of left ureteral orifice, flat, ulcerated, bleeding area on posterior wall in direct continuity	Transurethral biopsy and resection Patient well 9 months later

bladder. Diagnosis may be made by repeated cystoscopic examinations at short intervals and biopsy.

The proper treatment of this lesion when the location is appropriate is segmental resection. However, in five recorded cases transurethral resection has been performed and in three instances was successful. The use of irradiative methods does not appear to be a logical approach to the destruction of amyloid.

PRIMARY AMYLOIDOSIS OF THE SEMINAL VESICLES AND PROSTATE

The seminal vesicles, prostate, and testes were examined at autopsy in an unselected consecutive series of 167 male patients for the presence of amyloid. Of these, 129 patients were in the age group of 46 to 90 years.

Primary amyloidosis was found in the seminal vesicles of 2 patients, and in one of these it was also found in the prostate.

Mr. J. M., No. A49-197, a white man, aged 97 years, entered the Presbyterian Hospital on the service of Dr. Carl Davis, Jr. on August 17, 1949 with a complaint of left leg pain of 2 weeks' duration. Examination revealed a fracture of the neck of the left femur. He had urinary incontinence and an enlarged, hard prostate. Routine laboratory studies were essentially normal. The serum total proteins were 7.28 gm./100 cc; serum albumin, 3.38 gm./100 cc; serum globulin, 3.9 gm./100 cc; and A/G ratio 0.86 representing hyperglobulinemia. Treatment consisted of surgical approximation of the fracture and supportive care with death occurring on the sixth postoperative day.

The major findings at autopsy were: primary amyloid degeneration of the seminal vesicles and prostate; fracture of the neck of the left femur; basal cell carcinoma of the right ear; fat emboli of the lungs, spleen, and brain; adenocarcinoma of the prostate; and adenocarcinoma of the pancreatic duct.

The microscopic examination of the seminal vesicles revealed an amorphous, highly eosinophilic hyaline material in a layer beneath the mucosa (fig. 3, *A*). Occasionally irregular nodular deposits of this material were seen in the stroma of connective tissue and smooth muscle (fig. 3, *B*). This material gave the characteristic metachromatic reaction with crystal violet stain and the usual tinctorial reaction with Congo red.

Microscopic examination of the prostate revealed areas of benign hyperplasia and small areas of adenocarcinoma. A localized, rather sharply demarcated area of amorphous, highly eosinophilic hyaline material was seen lying in thick layers beneath the epithelium of the acini occasionally obliterating the acinar structures. There were also irregular nodular deposits in the smooth muscle stroma. This material gave characteristic stain reactions for amyloid with crystal violet and Congo red (fig. 4).

Mr. G. S., No. A49-190, a white man, aged 60 years, entered the Presbyterian Hospital on the service of Dr. A. A. Knight on August 2, 1949 for treatment of progressive cardiac decompensation of 6 months' duration. Physical examination revealed a dyspneic patient with marked enlargement of the liver and pitting edema of the lower extremities. The patient was anemic. Albumin, casts, and an occasional erythrocyte were found in the urine. The serum total proteins were 6.5 gm./100 cc; serum albumin, 3.24 gm./100 cc; serum globulin, 3.26 gm./100

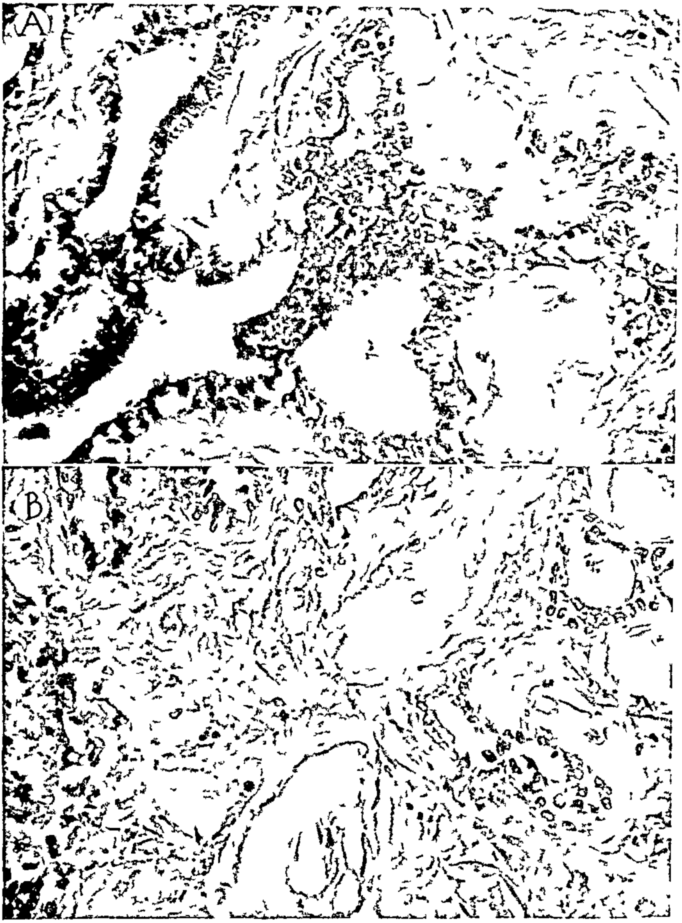

Fig 3 J M *A*, showing subepithelial deposition of amyloid in seminal vesicles of patient with primary localized amyloidosis of seminal vesicles and prostate *B*, showing nodular areas of amyloid deposition in connective tissue stroma of seminal vesicle

cc, and A/G ration, 0 99 representing definite hyperglobulinemia The hospital course was uneventful until the fourth day when the patient fell out of bed, became comatose, and died within twelve hours

Autopsy findings revealed a primary atypical amyloidosis with deposits in the seminal vesicles, thyroid, stomach, colon, pancreas, heart, adrenals, and spleen

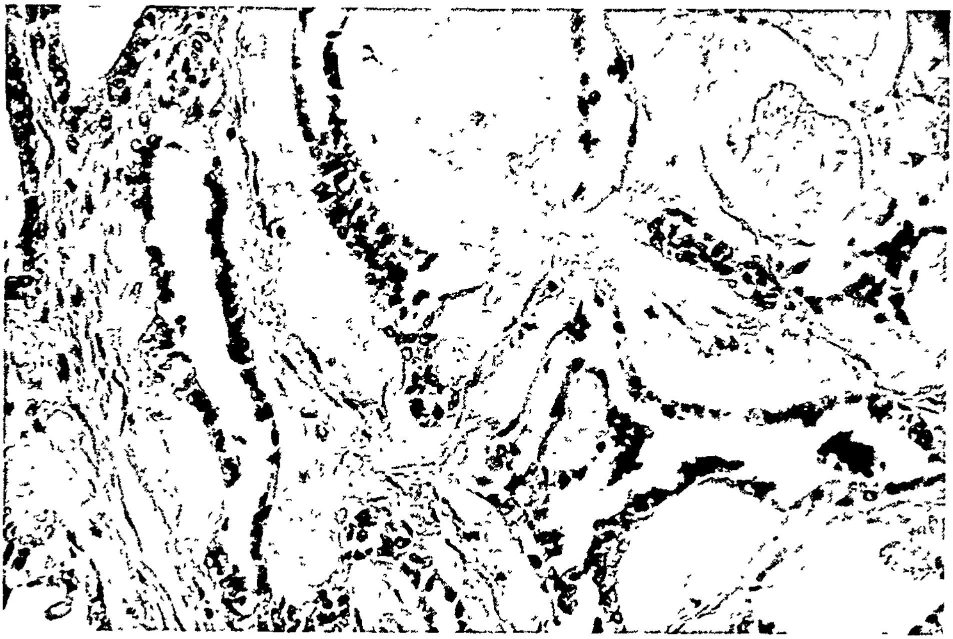

FIG. 4. J. M. Photomicrograph of prostate illustrating subepithelial and discrete nodular depositions of amyloid.

Microscopic examination of the seminal vesicles revealed a thick layer of homogeneous, amorphous, hyaline substance beneath the mucosa of the convoluted tubules with little tendency to extend out into the stroma (fig. 5). This material gave the characteristic reaction for amyloid with both crystal violet and Congo red stains.

Reference to primary localized amyloidosis of the seminal vesicles has appeared only in the German literature. Winklmann[28] reported 2 cases, and Erlach[29] added 3 cases. Lubarsch,[1] in his review of amyloidosis of the urinary tract, agreed that the occurrence of localized amyloidosis of the seminal vesicles is unusual and presented 1 case. Wassiljeff[30] reviewed 108 autopsies and found only one instance of localized amyloidosis of the seminal vesicles. Schonberg,[31] in a study of 50 cases at autopsy in 1948, found minimal amounts of amyloid in the seminal vesicles of only 4 patients. Dahlin,[6] in reporting 6 cases of primary systemic amyloid disease, found amyloid deposition in the vessels of the seminal vesicle of one patient. Lubarsch[14] noted similar deposits in two of 3 cases of primary systemic amyloidosis.

Bursell[32] reported 33 instances of localized amyloidosis of the seminal vesicles in 178 autopsy studies. Of these, 159 patients were over 50 years of age. He con-

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[29] Erlach, E.: Uber Amyloidablagerung in den Samenblasen. Arch. path. Anat., **272:** 418–429, 1929.

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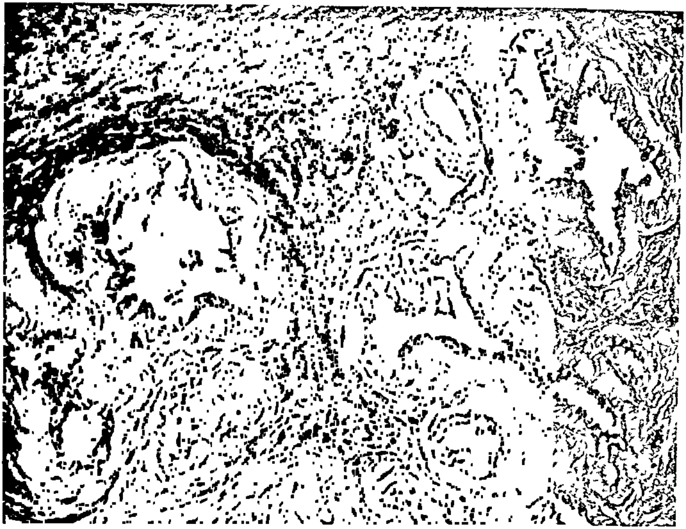

FIG. 5. G. S. Photomicrograph of seminal vesicle in patient with primary systemic amyloidosis. Section stained with crystal violet shows subepithelial deposition of amyloid.

cluded that subepithelial deposits of "paramyloid" in the seminal vesicles is a more or less common finding. He accounts for the low incidence in Wassiljeff's study on the basis that most of the patients were under fifty years of age. In an effort to explain the high incidence of this disease in his series, Bursell makes an association with the age groups. Although he found no amyloid in the seminal vesicles of patients under 46 years of age, he found 7.7 per cent in the group 46–60 years, 22.5 per cent in the group 61–75 years, and 34.2 per cent in the group 76–90 years. With the greater incidence of amyloid deposits occurring above the age of fifty, Bursell termed it "senile amyloidosis of the seminal vesicles."

Certainly the discrepancy in the findings of Bursell and those of Wassiljeff, Schonberg, and the present study indicates a need for further evaluation of a similar series of patients.

There are various opinions as to the etiology of amyloid degeneration of the seminal vesicles. Bursell feels it results from metabolic disturbances; Letterer,[32] from antigen-antibody reactions; Winklmann, from tissue malignancy; Schonberg, from reabsorption and deposition of a pre-amyloid type of secretion formed in the lumen of the convoluted tubules with the additional action of heparin. The hyperglobulinemia in each of the 2 cases presented here is of interest in the further consideration of the etiology. It is thought that amyloid may represent the tissue deposition of excess normal or abnormal globulin proteins. The occurrence of carcinoma of the prostate in association with local amyloid deposition in one of these patients gives further support to Winklmann's theory.

Of interest is the consideration of the possible clinical evidences of this disease as encountered in the seminal vesicles. Well known is the occurrence of hemorrhage in amyloid disease of the bladder and gastrointestinal tract.[33] It is possible that hemorrhage may occur from these lesions within the seminal vesicles. In the absence of other evidence to account for the hemorrhage, gross hematuria in the elderly generally has been ascribed to perforation of vessels in the prostatic urethra. It well may be that hematuria in the aged, in the absence of demonstrable evidence of a causative agent, may be due to the perforation of amyloid-weakened walls of blood vessels in the seminal vesicles.

Dahlin[6] has reported involvement of the prostate in systemic primary amyloidosis in 4 cases and Lubarsch in 2 cases,[15] while Villasenor[34] found similar involvement in 1 case. It is of interest as an unusual pathological feature but certainly of questionable clinical importance.

PRIMARY AMYLOIDOSIS OF THE URETHRA

While no instance of primary amyloidosis of the urethra was encountered in this study, mention of this rare form of the disease is necessitated by its clinical importance. The formation of localized tumor-like masses in the submucosa of the urethra produces obstruction. Involvement of the anterior, bulbomembranous, and the posterior urethra have been reported.[2, 17]

The diagnosis has been made only after histological examination of tissue removed by sharp curettment or by external urethrotomy. The end results of these two methods of treatment seem to be equally satisfactory.

SUMMARY

Primary localized amyloidosis of the bladder is a definite clinical entity with the principal characteristic of painless gross hematuria.

It is questionable whether primary amyloidosis of the seminal vesicles is of clinical importance.

The possible association has been made between amyloid degeneration of the seminal vesicles and prostate and gross hematuria in the aged.

The discrepancy in the reported incidence of primary amyloid disease of the seminal vesicles has been emphasized.

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THE JOURNAL OF UROLOGY
Vol 75 No 1 January 1956
Printed in U S A

CORTISONE IN THE TREATMENT OF EPIDIDYMITIS

THOMAS J FLORENCE

Epididymitis is one of the more troublesome conditions treated by the urologist It is manifested by marked incapacitation, severe pain, and prolonged morbidity The cause is probably inflammation proceeding from the region of the prostatic urethra by the vas deferens to the epididymis The possibility of hematogenous spread exists, but it is difficult to prove Much of the refractory nature and clinical course of this disease are due to the peculiar anatomy of the epididymis which consists of many circuitous coils and folds of a small duct encased in a dense covering Infection progresses rapidly to multiple areas of acute infection or even small abscesses that have no tubular outlet for drainage and inadequate ramification of vascular channels to absorb infection

The standard treatment for this condition is rest, elevation of the scrotum, analgesics, and antipyretics The question of heat or cold to the infected part is in dispute Along with many others, I prefer cold in the initial 1 to 3 days to abort infection and control pain and heat during the process of resolution Since the onset of the antibiotics, many have been tried My own impression is that they are of minimal value but possibly more efficacious if given at the immediate onset of inflammation A few cases require incision when definite large areas of fluctuation are present Incision of an enlarged epididymis *per se* does not hasten healing and is a troublesome nursing problem Occasional epididymo-orchiectomy must be done, rarely is epididymectomy performed in the chronic stage Tuberculous epididymitis should be extirpated if response to usual measures and streptomycin is not complete The value of vasectomy in the prevention of epididymitis is well known and should always be done unless contraindicated Infiltration of the spermatic cord with local anesthesia and aspiration of a concomitant hydrocele are useful "pearls" in patient comfort and acceleration of healing

In the past few months the unique and superlative qualities of cortisone and allied agents in the treatment of mumps orchitis stimulated an empirical use of cortisone* in combination with the newer antibiotics to routinely treat epididymitis Five cases are briefly abstracted

D E F , a 23-year-old white man, had acute right epididymitis He was first seen November 17, 1954 The cause was unknown He was treated by routine measures plus cortisone, penicillin, streptomycin and achromycin followed by rapid dissolution of pain and swelling On December 29, 1954, the testicle, epididymis, prostate, and urine were normal

D R J , a 28-year-old white man, was seen in the hospital on November 23, 1954 with right epididymo orchitis The cause was unknown He was treated

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Read at annual meeting Southeastern Section of American Urological Association, New Orleans, La March 20-24 1955

* In the cases reported here in abstract, cortisone was given by mouth every 6 hours for 5 to 10 days

Meticorten 5 mg by mouth every 6 hours, is now being used with equally good results and possibly less side effects by cortisone and achromycin followed by complete control of pain. By December 1, 1954 the epididymis, testicle, prostate, and urine were normal.

J. M. D., a 37-year-old white man, was seen in the office on January 21, 1955 with left acute epididymitis. Urinalysis showed many pus and blood cells and 2–3 plus sugar. He was treated by penicillin, streptomycin, achromycin and cortisone followed by prompt and steady improvement. The glycosuria responded to diet. On February 16, 1955 the testicle, epididymis and urine were normal.

B. T. M., a 32-year-old white man, was seen on January 25, 1955 with acute right epididymitis. He gave a past history of chills and fever, then urinary burning and frequency 2 weeks ago. Bloody ejaculation occurred the day previous to epididymitis. Urinalysis showed 50–100 white blood cells per high power field. Treatment consisted of penicillin, streptomycin, achromycin, elkosin, and cortisone. On February 4, 1955 the urine was normal and the scrotal contents normal.

L. G., a 37-year-old Negro, was seen February 3, 1955 with right epididymitis and acute hydrocele formation. Urine showed 20–30 white blood cells per high power field. Therapy instituted was aspiration of hydrocele, ice bags, penicillin, streptomycin, achromycin and cortisone. Healing was moderately slow but progressive.

In addition to the generally recognized procedures, cortisone was administered to each of these patients. The impression was that healing occurred faster and that pain and morbidity lessened. Cortisone has the quality of blocking body defenses in the walling-off of infection. It is postulated that in epididymitis early institution of cortisone inhibits the localization of infection and permits effective penetration by the antibiotics.

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The Journal of Urology
Vol 75, No 1, January 1956
Printed in U S A

THE SIGNIFICANCE OF HEMATURIA IN YOUNG MEN

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Few urinary difficulties send people scurrying faster to the physician than bloody urine Although a vast, virtually inexhaustible literature has accumulated emphasizing the importance of hematuria as a signpost pointing to lesions of great hazard, especially in the urologic tract, there apparently exists, as will be seen, considerable doubt and lack of appreciation of the merits of this belief, particularly regarding the young adult The following questions arise How often does hematuria occur in the young adult male? How much weight should one attach to it in this group? What are the probabilities that the underlying pathologic process is of grave consequence? How frequently is it caused by systemic disease?

Lowsley and Kirwin[1] expressed the prevalent opinion† when they said, "In well over 50 per cent of all cases of hematuria the blood is produced by urinary tract tumors, usually malignant, after tumor, calculus and tuberculosis are the most frequent exciting causes " They add that inflammations and stones predominate in the first four decades, tumors thereafter Nowhere, however, could a comprehensive answer, certainly none based on a statistical analysis, be found to the questions enumerated in the first paragraph This study was prepared in an effort to fill the gap

Between January 1, 1951 and November 30, 1953 it was the policy of the 141st General Hospital to admit all patients, whose primary or sole cause for hospitalization was gross or microscopic hematuria, to the urologic section An occasional patient did slip into the medical wards, but he was invariably transferred promptly Those cases of hematuria secondary to dramatic events, such as lancinating colic, overwhelming injury, all battle casualties, and where the bleeding was merely a phase of obvious, grave, systemic disease, like hemorrhagic fever, were not included in this analysis

During the aforementioned 35-month period, slightly more than 1200‡ noncombatant, male urologic patients were hospitalized, of whom 163 (about 13 6 per cent) came in because of blood in the urine This was the most frequent reason for admission, followed by painful scrotal swellings (152) and colic (146) These 163 men ranged in age from 18 to 53, but only three were over 41, there were 41 (25 15 per cent) under 21, 85 (52 15 per cent) between 21 and 30, and 34 (20 86 per cent) between 31 and 40 Slightly over 77 per cent of the patients were between 18 and 30, an age distribution corresponding to that of 529 out-

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Accepted for publication May 19, 1955

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† A complete bibliography would be many times more lengthy than the presentation Only those references have been used that either express the consensus of opinion, or confirm statements made

[1] Lowsley, Oswald S and Kirwin, Thomas J Clinical Urology Baltimore Williams and Wilkins Co , 1944

‡ Clinical abstracts were not kept on all patients discharged during January, February and March, 1951 The estimate was based upon a projection of the admission rates for the same 3 months of 1952, when troop strengths and climatic conditions were similar

patient men studied from the same locale,[2] and almost identical with the other 1050 odd noncombatant urologic casualties.

All of the 163 men were subjected to complete urologic investigation, consisting at least of an excretory urogram, cystoscopy, urine culture and determination of the antibiotic sensitivity reaction of the bacterial isolate. Twenty-two patients required surgery. In the occasional instance where this was not done at the 141st General Hospital, because of the then current tactical situation, followup notes were obtained from the institutions to which they had been evacuated.

Twenty-two patients (13.5 per cent) were admitted because of microscopic blood. In 16, this was found on a routine urinalysis done as part of an annual, or re-enlistment physical examination. The remaining six had gone on sick call with minor complaints: three because of dysuria and frequency, one each with vague suprapubic cramps, a little backache, and perineal distress. Twenty were promptly hospitalized; delays in the other two, 3 months in one, almost 6 in the other (see case 2), were due not to remissions on the part of physicians, but to obduration in the patients. In those with gross hematuria, the blood was invariably bright and fresh, only one instance exhibiting smoky and portwine urine (sickle cell anemia). In 78 (48.85 per cent) the passage of blood was unaccompanied by other difficulties, while 63 (38.65 per cent) complained of frequency, urgency, dysuria and suprapubic cramps, listed in the order of frequency. Excluding all obvious emergencies, *122 men with gross hematuria were referred to a urologist an average of one month after the onset of their bleeding.* Eight men with gross bleeding, in whom the source could not be found, were first seen by a urologist *3 months after the initiation of hematuria.*

Eighty men, almost half the series, were referred with a diagnosis of "acute glomerular nephritis." This was difficult to understand. Fishberg[3] did state that in the insidious onset of the disease "albumin, blood and casts were often the first evidence," and that "unusual very severe cases (may be) characterized by copious *hematuria and rapid progressive renal insufficiency* from the very start . . . ." (Italics, A. M. Fishberg.) However, nothing could be found to suggest the belief that acute glomerular nephritis is either the commonest, or even a very frequent cause of hematuria in any age group.

LESIONS PRODUCING HEMATURIA

Lower urinary tract infections proved to be the cause of bleeding in 112 men (68.71 per cent) (table 1). By far the commonest single etiologic process were the cystitides. In 49 of these, including the 2 cases of cystitis cystica, the infections were abacterial; coliforms were isolated in 9 others, and strains of Micrococcus pyogenes in three. In one case in which Escherichia coli were isolated the organism was sensitive to penicillin and all symptoms disappeared after the administration of 300,000 units of the drug. There was no difference clinically or endoscopically between the abacterial and bacterial cases, other than the two instances of cystitis cystica.

[2] Gartman, E. and Leibovitz, A.: I study of non-gonococcic urethritis, presumably venereal in origin, based upon 588 infections in 529 patients. Brit. J. Ven. Dis., 31: 92–97, 1955.

[3] Fishberg, Arthur M.: Hypertension and Nephritis. Lea and Febiger: Philadelphia, 1944.

TABLE 1. *Causes of hematuria in men between the ages of 18 and 53*

	Microscopic R.B.C.	Painless Gross	Painful Gross	Total	%
		Lower Tract			
Infections					
Posterior nongonococcic urethritis	8	15	4	27	
Posterior nongonococcic urethritis and basal cystitis	0	6	4	10	
Posterior nongonococcic urethritis limited to prostatic urethra	3	8	1	12	
Totals, nongonococcic urethritis	11	29	9	49	30.06
Acute hemorrhagic cystitis	1	17	41	59	
Cystitis cystica	0	0	2	2	
Totals, cystitis	1	17	43	61	37.42
Acute gonorrheal urethritis	0	2	0	2	1.23
Totals, infections	12	48	52	112	68.71
Other Nonsurgical Lesions					
Prostatic varices	0	3	0	3	
Stricture urethra	0	1	1	2	
Stricture urethral meatus.	0	1	0	1	
Totals	0	5	1	6	3.68
Totals, nonsurgical lesions	12	53	53	118	72.39
Surgical Lesions					
Bladder diverticulum (small)	0	0	1	1	0.63
Trauma					
Ruptured urethra	0	1	1	2	
Lacerations, pendulous urethra	0	2	0	2	
Totals	0	3	1	4	2.45
Tumors					
Papillary carcinoma of the bladder	1	1	2	4	
Intraurethral verruca	1	1	0	2	
Totals, tumors	2	2	2	6	3.68
Totals, surgical lesions	2	5	4	11	6.75
Grand totals, lower tract lesions.	14	58	57	129	79.14

TABLE 1. *Continued*

	Microscopic R.B.C.	Painless Gross	Painful Gross	Total	%
Upper Tract					
Infections					
Acute pyelonephritis	1	1	0	2	1.23
Other Nonsurgical Lesions					
Polycystic kidney disease..	1	1	0	2	
Sickle cell anemia	0	1	0	1	
Nephrosclerosis .	1	0	0	1	
Lower nephron nephrosis	0	1	0	1	
Totals	2	3	0	5	3.06
Totals, nonsurgical lesions . .	3	4	0	7	4.29
Surgical Lesions					
Ureteral stones.	2	1	4	7	
Calculous pyohydronephrosis	0	0	1	1	
Massive hydronephrosis	0	0	1	1	
Hydronephrotic ectopic kidney	0	1	0	1	
Massive hydrouretero- plus hydronephrosis due to ureterovesical stricture	1	0	0	1	
Totals	3	3	5	11	6.75
Trauma					
Contused kidney	0	5	0	5	
Ruptured kidney	0	0	1	1	
Totals, trauma	0	5	1	6	3.68
Tumors					
Benign solitary cyst of kidney	1	0	0	1	0.63
Totals, surgical lesions	4	8	6	18	11.05
Grand totals, upper tract..	7	12	6	25	15.34
Unknown	1	8	0	9	5.52
Grand totals, series	22	78	63	163	100.00
	(13.50%)	(47.85%)	(38.65%)		

The second most frequent cause was posterior nongonococcic urethritis. The fact that this disease may be complicated by hematuria has been generally overlooked. Harkness,[4] in his brilliant monograph on the subject, scarcely mentioned it. Yet it occurred in almost 3 per cent of 588 cases studied by Gartman and

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[4] Harkness, A. H.: Non-gonococcal urethritis. Edinburgh: E. and S. Livingstone, 1950.

Leibovitz[2]; the author saw a total of 2,267 cases in 35 months and there were 49 complicated by hematuria, or 2.2 per cent. Wherever there is a high concentration of lone young men, there is apt to be high incidence of nongonococcic urethritis and this must not be ignored in the differential diagnosis.

Of passing curiosity were the two young men in whom an acute gonorrheal urethritis was ushered in by violent bleeding. (See case 3.)

The other nonsurgical lesions of the lower tract were of no special importance.

Bloody urination as a cardinal symptom in ruptured urethra is very uncommon. The fact that these two men could void after their injuries led to almost fatal delays in hospitalization. One of the lacerations of the pendulous urethra resulted from cystoscopy, the other from excessive milking of the penis. Neither was of any consequence. Neither tumor nor stones were found in the diverticulum.

Four bladder tumors were found, all grade 1 papillary carcinomas. These occurred in a Negro of 20 (case 2), a Negro and Caucasian of 21 (case 1), and a white man of 22. Only one presented the classical picture of painless, admixed gross hematuria. Bleeding from intraurethral verruca occurred infrequently,[5] but these lesions occasionally invade the urethra extensively, even as high as the vesical outlet, and are often difficult to distinguish endoscopically from neoplasms.

The processes in the upper tract need little discussion. All were well recognized sources of bleeding. It should be pointed out, though, that hematuria was not a usual reason for seeking medical aid with stones; 129, all in the upper tract, were seen at the 141st General Hospital and the chief complaint in 121 was pain (102 colics, 19 with pain in one of the upper abdominal quadrants). The lower nephron nephrosis and two urethral stones in this series of 163 were produced by sulfadiazine (case 6). The one case of nephrosclerosis occurred in a Negro of 53, referred with a diagnosis of benign prostatic hypertrophy.

COMPARATIVE GRAVITY OF LESIONS CAUSING HEMATURIA

Twenty-two patients out of 163 admitted because of hematuria required surgery, or something less than 1 in 7; 26 of the lesions, almost 16 per cent, were grave enough to be considered potential hazards to life, while the incidence of malignant neoplasms was 24.5/1000. Three out of five of the other 1050 urologic patients required surgery at 141st General Hospital, but only 95 (9 per cent) of the lesions could be classed as endangering life, while only two malignant tumors, both of the testicle, were found, an incidence 1.91/1000. Thus *over twelve times as many* carcinomas were seen in patients admitted with hematuria than in urologic patients complaining of all other difficulties.

ILLUSTRATIVE CASES

Case 1. A 21-year-old white man was transferred to the Urologic Section January 7, 1951 complaining of recurrent episodes of terminal hematuria in conjunction with burning, frequency, urgency, stranguary, and suprapubic cramps for about three months. He had been treated intermittently by antibiotics for a lower urinary tract infection, and then admitted to the medical service with a diagnosis of acute glomerular nephritis. The usual battery of renal function studies, including an excretory urogram, disclosed no impairment in kidney function. At cystoscopic examination a papilloma, about 2 cm. long, was found springing from the left side of the trigone, just inside the vesical outlet. The tumor was resected endoscopically and proved to be a grade 1 papillary carcinoma. He was followed until separation from the service 18 months later and there was no recurrence.

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[5] Gartman, E.: Intraurethral verruca accuminata; a neglected entity. To be published.

Case 2. A 20-year-old Negro was evacuated from Korea on June 16, 1953 with no complaints. During the pre-embarkation physical examination 6 months earlier red blood cells had been found in his urine on several occasions. Before a complete evaluation could be done, the patient, who did not wish to leave his friends, was shipped overseas. A red bordered tracer was sent after him and it found him in a frontline fox-hole. He was evacuated through channels, the microscopic hematuria found at each institution en route. The tactical situation prevented further investigation in Korea.

A complete study was done at the 141st General Hospital. A long, pedunculated tumor was found arising from the posterior right lateral lip of the vesical outlet, almost filling the prostatic urethra. The patient was evacuated to the United States as expeditiously as possible because of the tactical situation. A subsequent report revealed the lesion to be a grade 1 papillary carcinoma. No further followup was obtained.

Case 3. A 23-year-old white man was admitted to the urologic section on February 26, 1952 complaining of violent, painless hematuria since arising. Physical examination disclosed a huge prostate and an irretractable prepuce. An excretory urogram demonstrated a normal upper tract, the cystogram a large prostatic filling defect. On grand rounds the afternoon of February 29, his prostate was palpated by all the visiting dignitaries, including the Surgeon General, AFFE, and a visiting urologic consultant from the United States. The next morning he awoke with a profuse urethral discharge, typical of gonorrhea, confirmed by smears and culture. Following treatment of his gonorrhea with penicillin the "neoplasm" disappeared. He was circumcised and discharged to duty.

Case 4. A 21-year-old white man was admitted to the urologic section August 17, 1951 complaining of terminal hematuria for one month, and frequency, urgency, and difficulty in voiding for 6 to 7 months. At 3 a.m. July 5, 1949, he had sustained fractures of the pelvis and left femur, for which he had been hospitalized 13 months, wearing an indwelling catheter for 8 months. Vesical calculi subsequently developed for which the patient underwent a suprapubic cystolithotomy in April 1950. The admitting diagnosis was recurrent bladder stones. A urologic investigation disclosed large right pyohydronephrosis with a collection of small stones in the inferior calyx, and a severe, fiery, secondary cystitis. The infective organism was Proteus mirabilis, resistant *in vitro* to all antibiotics. Right nephrectomy and subtotal ureterectomy were done with noteworthy ease

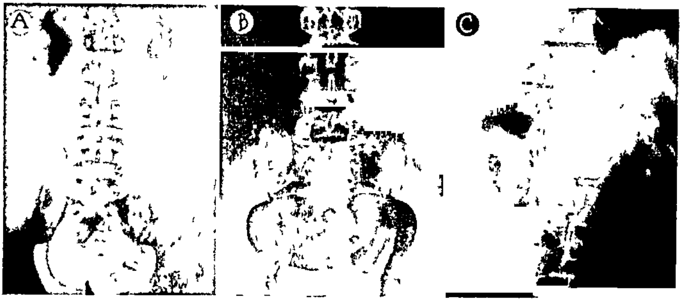

FIG. 1. A, preoperative retrograde pyelogram. B, detail of cystogram, 5 months postoperatively, showing reflux up unobstructed operated ureter. C, detail of retrograde pyelogram showing normal left kidney 6 months postoperatively.

August 29, 1951 under general anesthesia and the wound closed without drainage. No obstructive cause for the hydronephrosis was found. Convalescence was uneventful. Cystoscopy was repeated on his tenth postoperative day and the cystitis was gone. He was evacuated home primarily because of orthopedic difficulties September 10, 1951.

Case 5. A 19-year-old white man, a cook, was admitted to the Urologic Section May 11, 1953 because of the persistent finding of red blood cells in his urine, first noted during a semiannual food handler's examination. The patient considered himself in the best of health, but stated that he had been troubled with frequent backaches for the past 15 months, which he attributed to his work. A urologic investigation uncovered a large hydroureter and hydronephrosis, which took over 24 hours to empty, that was caused by a ureterovesical obstruction A similar, though milder lesion, which drained promptly, was also found on the right side (fig. 1, *A*). At surgery, May 25, 1953, a fusiform, spiral stricture of the intramural segment of the left ureter was found. This was corrected and a [illegible] left indwelling 6 weeks. Convalescence was uneventful. Following [illegible] duty July 18, 1953 he was dilated regularly for 4 months, at which time [illegible] complete resolution was found (fig. 1, *B* and *C*). He no longer complains of backache.

Case 6. A 20-year-old white man was flown into the urologic [illegible] evening of August 18, 1953 complaining of violent, painless hematuria [illegible] followed by suprapubic cramps and then inability to void for over 60 [illegible] troubles began when acute, right epididymitis developed 10 days [illegible] which he had been given a bottle of sulfadiazine. The weather was [illegible] the patient did heavy manual labor and averaged about 5 gm. of [illegible] He first saw blood in his urine August 12 and informed one of [illegible] physicians of this, but the drug was not stopped until August [illegible] of August 15, his urine suddenly became "black with blood [illegible] with knife-like suprapubic cramps. He was admitted to [illegible] cystoscopy; sulfadiazine crystals were washed from both [illegible] fluids were pushed. He did not void again, nor was any urine found in his bladder, after 8 a.m., August 16, 1952.

The patient was acutely ill, mildly uremic, and had diffuse anasarca associated with marked pulmonary edema. His temperature was 101.2F, blood pressure 140/80, the blood urea nitrogen 28.5 mg. per cent, the blood sulfadiazine level 3.4 mg. per cent. An indwelling catheter was inserted. The bladder was empty. The chaplain was summoned, absolution granted, and all three prayed for the patient's life. Shortly after the chaplain left, urine began dribbling out the catheter. The patient then was placed on 25 cc tap water by mouth every 2 hours and the output, in first 8 hours, was 1000 cc on an intake of 125 cc. By the end of the first day he had put out 1800 cc on an intake of 825 cc. He was now afebrile, the anasarca and pulmonary edema gone. Subsequent studies showed no renal damage.

SUMMARY

In a series of over 1200 young, noncombatant male urologic casualties, 163 were admitted because of hematuria, the most frequent reason for admission. One hundred eighteen of these men had relatively innocent lesions of the lower tract.

No cases of acute glomerular nephritis were found, although this was the commonest transferring diagnosis.

In only 5 patients was the cause of the bleeding outside the province of urologic surgery.

Twenty-six patients, almost 16 per cent, had underlying pathologic processes inimical to life. Only 9 per cent of the other 1050 odd urologic patients had lesions of comparable gravity.

The expectant malignant neoplastic rate in patients complaining of hematuria was 24.5/1000, while it was only 1.91/1000 in the other urologic patients, a ratio of more than 12 to 1.

CONCLUSION

Hematuria in the young man warrants a prompt, complete urologic investigation in all instances.

The Journal of Urology
Vol 75 No 1, January 1956
Printed in U.S.A.

THE USE OF L-TARTRATE IN DETERMINING "PROSTATIC" SERUM ACID PHOSPHATASE. A REPORT OF 514 CASES

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Interest in serum acid phosphatase has increased considerably since Gutman and Gutman[1] in 1938 first reported elevated levels of the enzyme in patients with metastases from carcinoma of the prostate. Gutman[2] in 1940 found that 84 per cent of patients with prostatic carcinoma with metastases had an elevation of serum acid phosphatase. Woodard[3] in 1952 reported 74 per cent of such patients had an elevated serum acid phosphatase, but 20 per cent of patients with widespread metastases failed to show any elevation of the serum acid phosphatase. The latter observation, she believes is due to certain types of prostatic carcinoma which produce too little phosphatase to be demonstrated in the serum.

A few urologists today have abandoned the serum acid phosphatase determination in patients with carcinoma of the prostate. Since positive levels are most commonly found in patients with obvious carcinoma and typical osteoblastic metastases, the diagnosis is apparent on rectal examination, plain x-ray of the spine and pelvis, and surgical biopsy. The test would be more valuable if significant elevations were 1) specific for carcinoma of the prostate and 2) found to be present before extensive metastases have occurred. Woodard[3] found elevated total serum acid phosphatase in only 5 per cent of carcinomas confined to the prostate gland and in 31 per cent of locally invasive prostatic carcinomas. Delory, Sweetser and White[4] in 1951 showed that elevated total serum acid phosphatase is not pathognomonic of carcinoma of the prostate. They reported elevated levels in 5 out of 29 cases of cancer other than prostatic, in 13 out of 36 cases of diseases of the liver and bile tract, in 2 out of 12 cases with various kidney diseases, in 1 out of 9 cases of Paget's disease and in 5 out of 29 miscellaneous diseases, such as bronchopneumonia.

The normal amount of serum acid phosphatase arises from liver, spleen, bone and kidney tissue as well as from the prostate gland. Hemolysis of red blood cells can produce elevation of total serum acid phosphatase and, thus, give "false positive" results.

Read at annual meeting, Southeastern Section of American Urological Association, New Orleans, La. March 20–24, 1955.

Aided in part by a grant in aid from the National Cancer Institute of the United States Public Health Service, Bethesda, Maryland.

[1] Gutman, A. B. and Gutman, E. B.: An "acid" phosphatase occurring in the serum of patients with metastasizing carcinoma of the prostate gland. J. Clin. Invest., **17**: 473–478, 1938.

[2] Gutman, A. B., Gutman, E. B. and Robinson, J. N.: Determination of serum "acid" phosphatase activity in differentiating skeletal metastases secondary to prostatic carcinoma from Paget's disease of bone. Am. J. Cancer, **38**: 103–108, 1940.

[3] Woodard, H. Q.: Factors leading to elevations in serum acid glycerophosphatase. Cancer, **5**: 236–41, 1952.

[4] Delory, G. E., Sweetser, T. H., Jr. and White, T. A.: The use of formalin and alcohol in estimation of prostatic phosphatase. J. Urol., **66**: 724–733, 1951.

In 1949 Abul-Fad'l and King[5] found that the acid phosphatase liberated by hemolysis could be destroyed by adding 2 per cent formalin to the incubating mixture without affecting the "prostatic" acid phosphatase. Conversely, Fad'l and King noted that the prostatic enzyme could be inhibited by adding L-tartrate to the incubating mixture.

Delory, Sweetser and White[4] tested the use of formalin in obtaining "prostatic" acid phosphatase and recommended that its use be routine in order to eliminate errors due to hemolysis.

METHOD

Fishman and Lerner[6, 7] have described the method of determining "prostatic" acid phosphatase by the L-tartrate method. The hydrolysis of phenyl-phosphate is measured in the absence and in the presence of L-tartrate. The difference found in the amount of phenol liberated is believed to represent the inhibition of acid phosphatase of prostatic origin. Total acid phosphatase and "prostatic" acid phosphatase are expressed in King-Armstrong units, the "prostatic" acid phosphatase representing that amount of the total acid phosphatase which is inhibited by L-tartrate.

The normal range for total acid phosphatase is 0.5 to 3.5 King-Armstrong units. Fishman and Lerner[7] have tentatively set 0–0.5 units as the normal range for "prostatic" acid phosphatase obtained by the L-tartrate method because none of their 150 control cases had levels above 0.5 units. They found that of 12 untreated cases of carcinoma of the prostate, 7 with metastases had elevation of both total and "prostatic" acid phosphatase. The 5 cases without metastases had normal total acid phosphatase whereas the "prostatic" acid phosphatase was elevated in 4 of these cases. Of 8 cases of carcinoma of the prostate which were controlled by estrogen therapy, all had normal total acid phosphatase, and 7 had normal "prostatic" acid phosphatase, 1 being elevated to 0.7 units. They conclude, therefore, that the L-tartrate inhibited acid phosphatase is largely of prostatic origin and that it parallels total acid phosphatase changes during hormonal therapy, yet appears to be more sensitive.

The present study is a comparison of the total and "prostatic" serum acid phosphatase levels on 514 patients seen in John Gaston Hospital, West Tennessee Cancer Clinic and the Urology Out-Patient Department, using Fishman and Lerner's technique for determining the L-tartrate inhibited "prostatic" acid phosphatase

RESULTS

1. Controls. Two hundred and thirty-four women and 160 men with no prostatic disease were examined, a total of 394 control cases including a large variety of medical and surgical diseases and nonprostatic malignancies. Of the 234

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[5] Abul-Fad'l, M. A. M. and King, E. J.: Properties of the acid phosphatase of erythrocytes and of the human prostate gland. Biochem. J., **45**: 51–60, 1949.

[6] Fishman, W. H. and Lerner, F. A.: A method for estimating serum acid phosphatase of prostatic origin. J. Biol. Chem., **200**: 89–97, 1953.

[7] Fishman, W. H., Dart, R. M., Bonner, C. D., Leadbetter, W. F., Lerner, F. and Homburger, F.: J. Clin. Invest., **12**: 1034–1044, 1953.

TABLE 1. *Phosphatase on female patients*
234, total women examined
218, normal range
16, "prostatic" acid phosphatase above 0.5 units
2, "prostatic" acid phosphatase above 0.8 units

Diagnosis	Serum Acid Phosphatase	
	Total	"Prostatic"
Senile keratosis	1.4	1.05
Fibroadenoma	1.65	0.65
Hyperkeratosis	2.5	0.55
Leukoplakia, buccal mucosa	1.7	0.6
Ca. cervix	1.5	0.55
Tubo ovarian abscess	2 65	0 6
Ca. cervix post-radiation	2.4	0 7
Rectal fistula	2.6	0.55
Rectal stricture	2.3	0.7
H C V D	2 6	0.65
Ca cervix	1 50	0.6
Uremia	4 80	1 0
Pneumonia	2.25	0.6
Fibroid uterus	1.90	0 55
Fibroid uterus	0 80	0 60
Myeloid leukemia	1 65	0.70

women examined (table 1), 16 gave values above 0.5 units for "prostatic" acid phosphatase, and only 2 were above 0.8 units. Of the 160 men without known prostatic disease, 16 had "prostatic" acid phosphatase levels above 0.5 units, while only 6 had levels above 0.8 units (table 2). The total results show that only 8 of the 394 control patients (2 per cent) had "prostatic" acid phosphatase levels above 0.8 units, whereas 32 (8 per cent) were above 0.5 units.

We, therefore, infer that 0.8 units should be the upper limit of normal for "prostatic" acid phosphatase. This level will be further demonstrated in cases of benign prostatic hypertrophy. Although we have been unable to recheck the cases, the 8 elevations above 0.8 units were probably due to laboratory error or temporary elevation of serum acid phosphatase following digital prostatic examination.

2. Benign prostatic hypertrophy. Seventy cases of benign prostatic hypertrophy proven by surgery were examined Total acid phosphatase ranged from 0.50 to 3.10 King-Armstrong units, all within the normal range. The "prostatic" phosphatase ranged from 0.10 to 0.80 units. Thirteen of the 70 had "prostatic" acid phosphatase levels over 0.5 units, but none had levels above 0.8 units.

3. Carcinoma of the prostate. Fifty cases of carcinoma of the prostate were examined. The level of serum acid phosphatase is dependent upon a) the presence of metastases, b) local extension of the cancer beyond the capsule, and c) the degree of control achieved by hormonal therapy. These 50 cases, therefore, have been classified into two main groups: those not receiving hormonal therapy (table 3) and those who have had orchiectomy or are receiving stilbestrol (table

TABLE 2. *Phosphatase run on male patients*

160, control patients with no prostatic disease
154, normal range ("prostatic" acid phosphatase under 0.8 units)
15, "prostatic" acid phosphatase above 0.5 units
6, "prostatic" acid phosphatase above 0.8 units

Diagnosis	Serum Acid Phosphatase	
	Total	"Prostatic"
Myeloid	2.30	0.75
Tuberculosis	1.35	0.55
Pneumonia	3.45	0.70
H C V D; cardiac insufficiency	4.40	1.35
Pneumonia	2.10	0.60
H C V D	2.75	0.60
Broncho. ca. lung	2.30	1.00
Fracture	3.51	0.60
Arteriosclerotic vascular disease	2.55	0.65
Rupture spleen and liver	2.50	0.70
Stab wound	3.50	0.70
Gastric ulcer	3.55	1.00
Nephrosis	4.50	0.90
Chronic osteomyelitis	3.30	1.80
Ca. colon	2.35	1.25

TABLE 3. *Patients with carcinoma of the prostate receiving no hormonal therapy*

Patient	Carcinoma Proven by Prostatectomy	Acid Phosphatase	
		Total	Prostatic
1. With metastases			
A. B.	+	5.60	3.70
W. N.	+	6.50	3.30
C. D.	−	44.30	31.50
B. L.	−	24.40	21.90
J. M.	−	1.65	0.82
J. A.	−	3.45	2.85
2. Without metastases			
R. D.	+	1.55	0.20
G. F.	+	2.65	1.15
R. P.	+	2.50	1.30
E. A.	−	3.70	1.30
J. W.	+	4.75	2.55
C. K.	−	3.55	2.10
J. W.	+	4.90	2.45
B. M.	+ (Radical)	1.90	0.35
F. R.	−	1.50	0.10
F. C.	+	5.60	4.40
J. H.	+	2.10	1.80

TABLE 4. *Patients with carcinoma of the prostate receiving hormonal therapy*

Patient	Prostatectomy	Orchiectomy	Stilbestrol	Serum Acid Phosphatase	
				Total	"Prostatic"
1. With metastases					
T. M.	+	−	3 mos.	6.36	1.74
E. M.	+	+	4 yrs.	1.14	0.60
A. M.	+	+	18 mos.	2.15	0.45
M. S.	+	−	3 yrs.	2.15	0.80
A. M.	+	+	12 mos.	3.40	1.50
W. B.	+	−	12 mos.	23.20	20.70
H. B	−	−	10 mos.	6.24	3.48
W. H.	−	+	12 mos.	2.70	1.14
H. J.	−	−	8 mos.	1.25	0.20
W. J.	−	−	3 yrs.	21.30	19.70
F. S.	−	−	4 mos	1.10	1.07
M. A.	+	−	8 mos	48.45	44.10
W. M.	−	+	1 wk	3.30	1.13
P. M.	+	−	2 yrs.	49.20	42.60
C. B	−	+	9 mos.	3.15	1.35
E. L. C.	+	+	3 yrs.	44.9	41.2
2 Without metastases					
J. A.	+	−	5 yrs.	2.55	0.30
O. A.	+	−	9 mos.	1.55	0.45
H. M.	+	+	6 mos	1.35	0.38
J. N.	+	−	9 mos.	6.40	1.30
C. R	+	+	2 mos.	1.25	0.20
R. S.	+	+	2 yrs.	1.95	0.65
C. T.	+	−	6 mos	1.00	0.25
E. W	+	−	11 mos.	1.45	0.30
F. H.	−	−	3 mos.	0.40	0.0
B. P.	−	−	6 mos.	2.00	0.45
A. S.	−	−	8 mos.	1.55	0.45
M. C. P.	−	−	3 mos.	3.90	0.60
A. G.	−	−	9 mos.	1.50	0.53
C. W.	+	+	3 yrs	1.43	0.30
H. W	+	+	1 yr	1.58	0.90
G. B.	+	−	9 mos.	2.48	0.45
W. P. P.	+	+	3 yrs.	1.20	0.15

4). Each of these tables is subdivided into groups of patients with metastases and those without metastases, as demonstrated by x-ray examination of the pelvis, spine and lung fields.

Thirty-one of the 50 cases were proven carcinoma by pathological examination following surgery. Clinically the remaining 19 cases were carcinoma, 11 of which had definite osteoblastic metastases. The "prostatic" acid phosphatase was elevated (0.8 units or above) in 29 (58 per cent) of the 50 cases, while only 17 (34 per cent) had elevated total acid phosphatase (over 3.5 units).

Of the group receiving no hormonal therapy at the time of examination, there were 6 with metastases. The "prostatic" acid phosphatase was elevated in all 6 cases (100 per cent), and the total acid phosphatase was elevated in 4 (66 per cent) of the 6 cases (table 3, part 1). Eleven patients in this group had no demonstrable metastases, but the cancer was locally invasive in all but 1 of these patients. This single patient (table 3, case 8) had normal total and "prostatic" acid phosphatase, as one would expect in an early carcinoma of the prostate. He was treated by radical prostatectomy. All the other surgical cases were handled transurethrally to relieve obstruction and to confirm the diagnosis. Excluding this 1 case of early carcinoma, there were 8 of the 10 (80 per cent) patients with local invasion only who had elevation of the "prostatic" acid phosphatase, while only 5 (50 per cent) had elevated total acid phosphatase (table 3, part 2). This figure of 80 per cent positive cases is considerably higher than Woodard's 31 per cent positive for locally invasive untreated cases.

The second group is composed of 33 patients who were receiving hormonal therapy at the time of examination. Twelve had undergone orchiectomy, and all were receiving from 5 to 25 mg. of stilbestrol daily. It is not the purpose of this paper to study the effect of hormonal therapy in controlling carcinoma of the prostate. However, it has long been recognized that the acid phosphatase level often serves as an indicator of the amount of control obtained by hormonal therapy. This fact may be demonstrated in the 17 patients without metastases on hormonal therapy (table 4, part 2), only 2 (12 per cent) of whom had elevated serum acid phosphatase, total and "prostatic." Thus, 80 per cent of the untreated cases (table 3, part 2) of locally invasive carcinoma had elevated "prostatic" acid phosphatase, and only 12 per cent of the treated cases showed any elevation.

Of the 16 patients receiving hormonal treatment who had metastases at the time of examination (table 4, part 1), the "prostatic" acid phosphatase was elevated in 13 (80 per cent), whereas only 7 (43 per cent) had elevated total acid phosphatase. In these cases hormonal therapy may have still been producing relief of pain, or the carcinoma may have escaped from the temporary control achieved by hormonal management. The high acid phosphatase indicates, nevertheless, that the carcinoma was still active in spite of hormonal therapy.

By combining all the cases with metastases (part 1 of tables 3 and 4) there are 22 patients, 19 of whom (86 per cent) had an elevation of "prostatic" acid phosphatase, while only 11 (50 per cent) showed elevation of the total acid phosphatase. Of the 28 patients without metastases, 10 (36 per cent) had elevated "prostatic" acid phosphatase, and 7 (25 per cent) had elevated total acid phosphatase.

DISCUSSION

With comparison of the two methods of determining acid phosphatase the L-tartrate inhibited "prostatic" acid phosphatase was found to be positive in about 30 per cent more cases than the total acid phosphatase in the above groups. In the first group there were 17 patients who were not on hormonal therapy, 14 (82 per cent) of whom had elevated "prostatic" acid phosphatase, while only 9 (53 per cent) had elevated total acid phosphatase using the King-Armstrong method of determination. In the second group of 33 patients on hormonal therapy, 14 (45 per cent) gave positive "prostatic" acid phosphatase levels while 9 (27 per cent) had positive total acid phosphatase. One case of particular interest (W. H., table 4) had a "prostatic" acid phosphatase of 1.14 units when first seen. Orchiectomy was performed for palliation and stilbestrol was given. Two months later the "prostatic" acid phosphatase fell to 0.35 units. During the same period the total acid phosphatase was always in the normal range.

4. Effect of estrogens. To determine if estrogens in the serum of patients receiving hormonal therapy had any direct inhibitive effect upon serum acid phosphatase, 1 mg. of estrogen (neo amniotin, Squibb) was added to the substrate in 6 patients not receiving stilbestrol orally. Instead of a decrease, a slight elevation occurred in the 6 cases checked, suggesting that there is no direct inhibition from estrogens.

Patients Not on Estrogen Therapy, Total Acid Phosphatase	After Addition of Estrogen Total Acid Phosphatase
units	*units*
2.7	2.98
2.45	2.96
3.85	4.15
5.6	6.1
1.65	2.40
2.4	2.9

5. Administration of testosterone. Fifty milligrams of testosterone propionate were given intramuscularly to 6 patients, and total and "prostatic" acid phosphatases were repeated 2 hours after the injection. Three patients had benign prostatic hypertrophy and 3 had prostatic carcinoma. It was hoped that the ad

Benign prostatic hyperplasia

Acid phosphatase

Before Giving Testosterone		Two Hours after Testosterone	
Total	Prostatic	Total	Prostatic
units	*units*	*units*	*units*
1.90	0.8	1.90	0.6
1.80	0.7	1.70	0.6
1.80	0.35	1.10	0.2

Carcinoma of prostate

Acid phosphatase

Before Giving Testosterone		Two Hours after Testosterone	
Total	Prostatic	Total	Prostatic
units	*units*	*units*	*units*
3.70	1.30	1.10	0.45
1.45	0.3	1.30	0.4
3.10	0.06	1.10	0.2

ministration of testosterone would raise the level of acid phosphatase in carcinoma from a doubtful range to a positive range without influencing the level in benign prostatic hypertrophy. However, no significant effect was noted in either group.

SUMMARY

A study of the total and "prostatic" serum acid phosphatase of 514 patients has been presented with a comparison of the two determinations. The L-tartrate inhibitor method of Fishman and Lerner was employed in determining the "prostatic" enzyme in the serum of 394 control patients and 120 cases with prostatic disease.

"Prostatic" acid phosphatase levels up to 0.8 King-Armstrong units were found to be present in normal subjects and many women, the enzyme probably originating in the spleen, liver and normal male prostate gland.

Elevations above 0.8 units for the "prostatic" acid phosphatase did not occur in 70 cases of benign prostatic hyperplasia. Two per cent of the 394 control patients had elevations above 0.8 units, probably due to laboratory error.

The acid phosphatase inhibited by L-tartrate appears to arise predominantly from the prostate gland and from carcinoma of the prostate gland and its metastases.

The "prostatic" acid phosphatase appears to be 30–40 per cent more sensitive than total serum acid phosphatase. Of 16 cases of carcinoma of the prostate with metastases on hormonal therapy, the "prostatic" acid phosphatase was elevated in 13 (80 per cent) patients, and the total acid phosphatase was elevated in only 7 (43 per cent). Of 10 patients without metastases receiving no hormonal therapy, 8 (80 per cent) had elevated "prostatic," and only 5 (50 per cent) had elevated total serum acid phosphatase.

"Prostatic" total acid phosphatase was elevated in all 6 cases of untreated prostatic carcinoma with metastases. Both total and "prostatic" acid phosphatase were elevated in only 2 of 17 patients with carcinoma of the prostate limited to the gland and the periprostatic tissues and clinically controlled by hormonal therapy.

The addition of 1 mg. of estrogen to the serum of 6 patients not receiving hormonal therapy produced no reduction of the total acid phosphatase level. The indication is, therefore, that estrogen does not directly inhibit serum acid phosphatase.

The administration of 50 mg. testosterone propionate intramuscularly did not produce any significant rise in total or "prostatic" acid phosphatase which was determined before and two hours after injection of the hormone.

We wish to thank Drs. Thomas D. Moore and Samuel L. Raines, professors of urology, University of Tennessee, for their encouragement and assistance with this study.

THE JOURNAL OF UROLOGY
Vol. 75, No. 1, January 1956
Printed in U.S.A.

CYSTOGRAPHY IN CHILDREN

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The usual indication for urological investigation in the infant or child is some symptom of vesical dysfunction. Infection may or may not be present. Whereas the information gained from careful cystourethroscopy and pyelography is not to be minimized, the value of routine cystography as a radiographic study of vesical function in the child cannot be overly emphasized. The demonstration of enlarged bladders, trabeculation, cellules, residual urine and vesicoureteral reflux is clear cut.

Cystography is not new, only some of the techniques. Unfortunately, the procedure has been rusting on the shelf. Thanks to Charles M. Stewart,[1] delayed cystography was introduced in 1948. He and Bunge[2] have now reported large series with valuable clinical observations. Bors[3] and Hutch[4] have utilized cystography in the radiographic study of vesical function in the paraplegic. Hinman[5] and Benjamin[6] have studied micturition and vesicoureteral reflux by serial roentgenography and cinefluorography, procedures certainly worthy of experimental value but unavailable to the average urologist.

PROCEDURE

This method has been followed and is done, if feasible, at the time of the initial office consultation. Small doses of demerol help control the smaller child. The patient is catheterized for residual after voiding, the bladder is then filled by gravity until the patient feels full or the liquid level begins to waver up and down in the barrel of the syringe. A film is made which is termed the "gravity cystogram." The catheter is then removed and the patient is again urged to void. A film made during voiding is taken in the older child. In the smaller tot, where voiding is cumbersome in the supine or semi erect position, the patient is allowed to stand or sit. Immediately after micturition is complete, a film is taken and termed "post voiding cystogram." An emptying film is taken if reflux demonstrates a tortuous ureter. The remainder of the urological examination, cystourethroscopy and pyelography, is completed subsequently.

Admittedly this simplified procedure has its inadequacies. It necessitates some pain for the child, but willful co operation is still present and there is no questionable effect of a general anesthetic upon the findings. Sodium iodide, 5 per cent solution, is cheap, nonirritating, yet not always opaque enough for good

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Read at annual meeting, Southeastern Section of American Urological Association, New Orleans, La., March 20–24, 1955.

[1] Stewart, C. M.: Delayed cystograms. J. Urol., 70: 588–593, 1953.

[2] Bunge, R. G.: Further observation with delayed cystograms. J. Urol., 71: 427–434, 1953.

[3] Bors, E. and Comarr, A. E.: Vesico ureteral reflux in paraplegic patients. J. Urol., 68: 691–698, 1952.

[4] Hutch, J. A. and Bunts, R. C.: The present urological status of the wartime paraplegic. J. Urol., 66: 218–228, 1951.

[5] Hinman, F., Jr., Miller, G. A., Nickel, F. and Miller, E. A.: Vesical physiology demonstrated by cineradiography and serial roentgenography. Radiology, 62: 713–719, 1954.

[6] Benjamin, J. A., Joint, F. T., Ramsay, G. H., Watson, J. S., Weinberg, S. and Scott, W. W.: Cinefluorographic studies of bladder and urethral function in human and dog. J. Urol., 73: 525–535, 1955.

slide reproduction of vesicoureteral reflux. This regurgitation may be occasionally missed if there is too much delay in getting the post-voiding film, as the dye may go up and down the ureter rapidly.

CLINICAL STUDY

Gravity cystograms had been used sporadically by the authors in the past and were confined to some particular problem as J. B., a white boy, aged 5 years. He was first seen on January 2, 1954, with fever and pyuria. Diurnal incontinence had been present all of his life. Neither this nor his urine had ever been investigated. The nonprotein nitrogen was 37 mg. per cent, but there was no appearance of dye even in 4 hours after injection of neo-iopax. Instead of proceeding to cystoscopy, it was felt safer to utilize a less traumatic procedure first, one which might establish the diagnosis. Catheterization recovered 350 cc residual. A gravity cystogram revealed marked vesicoureteral reflux (fig. 1).

Thanks to the stimulus of Orvar Swenson, personal experience with voiding cystography began on March 17, 1954. The first two cases studied are presented as follows: Case 1. R. W., a white boy aged 10 years, was referred by another urologist for consultation. Removal of the right kidney had been advised; the parents wished another opinion. The history was that of mild pyuria twice and dysuria once. The examination revealed no residual urine, normal gravity cystogram, failure of the right kidney to visualize in 30 minutes by excretory urography, and no appearance of indigo carmine in 15 minutes. A retrograde pyelogram suggested an atrophic pyelonephritis and a nephrectomy had been recommended. This workup certainly seemed adequate enough, yet a voiding cystogram revealed a dilated posterior urethra, marked regurgitation of medium up the right ureter, a normal sized kidney and engorged pelvis. Obviously there was infravesical obstruction. He was returned to his urologist. A retropubic resection of the bladder neck was done, and 5 months later, there was good return of function to the right kidney.

Case 2, T. H., a white boy aged 7 years, was referred for diurnal incontinence and recurrent left pyelonephritis. One year previously, a urologist examined him and the patient was dismissed because no pathological process was found. Excretory urograms were repeated. There was no change, and they were considered normal. He voided with a good stream, and there was no residual. However, a voiding cystogram (fig. 1) revealed marked reflux up the left ureter. This certain bladder neck obstruction was not readily apparent on endoscopic examination, even with the aforementioned information. True, the bladder was trabeculated, but it required "sitting on" the infant McCarthy cystourethroscope to allow full distention of the bladder and posterior urethra before the fibrosis in the median bar could be demonstrated. Frankly, this slight degree of bladder neck obstruction seemed incapable of producing such a marked degree of reflux and would not have been evaluated as such without the cystographic findings.

The demonstration of vesicoureteral reflux in four of the first seven children subjected to voiding cystography prompted its routine usage. In the 10 months

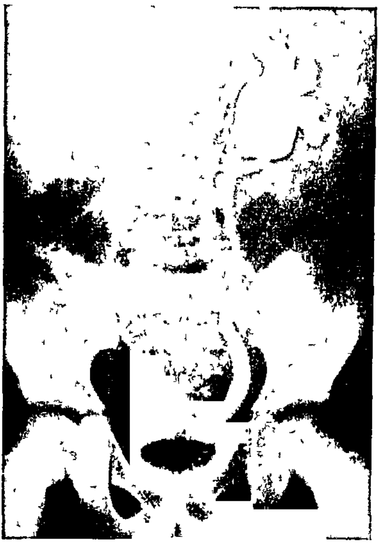

FIG. 1. Case 2. Post-voiding cystogram showing marked left vesicoureteral reflux.

from March 1954 to January 1955, a total of 100 children were given complete urological examinations. Sixty were girls, 40 boys. Seventy-four were new patients, 26 were old. An evaluation of the findings forms the basis of this report.

CLINICAL FINDINGS

Estimation of normalcy of bladder size is sometimes difficult. As a rule, most children held more fluid than stated in Campbell's text.[7] The bladder was considered enlarged in 12 patients. Whereas trabeculation was seen 70 times endoscopically, this was found only twice in the gravity cystogram or full bladder. In the post-voiding film, trabeculation was readily demonstrable as a "wrinkling effect" in the 22 patients with residual dye plus endoscopic evidence of trabeculation. Two patients had a diverticulum of the bladder.

Vesicoureteral reflux in 20 children: 16 girls, 4 boys. Whereas 14 cases of ureteral reflux were detected in the gravity cystogram, an additional 6 cases were demonstrated in the voiding or post-voiding film. Unilateral reflux became bilateral in 1 patient after micturition. Therefore, the incidence of reflux was 50 per cent higher when the act of micturition was initiated and the necessary intravesical pressure of voiding against an obstruction was developed. Three girls showed slight reflux in the gravity cystogram, but were able to empty this and the bladder completely in the post-voiding film. This could be explained on previous dilatations of the urethra. In no patient was reflux found where there were not other endoscopic findings of infravesical obstruction. Chronic infection of the bladder contributed to valvular incompetence in 3 cases. Size of the ureteral orifice gave no indication of reflux. It occurred with orifices of normal size in most patients. Also reflux could not be demonstrated in some patients having conspicuously large orifices.

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[7] Campbell, M.: Clinical Pediatric Urology. Philadelphia: W. B. Saunders Co., 1951.

Of particular interest was a group of 4 females with unilateral reduplication of ureters and pelves plus bladder neck obstructions. Vesicoureteral reflux to the lower half of the kidney occurred in all 4 cases. Above the end of the ureteral ridge was a saccule when the bladder was distended. It is postulated[8] that this sacculation is a weakness in the bladder wall existing posterior to the intramural portion of the upper ureter. Reflux occurs because there is no longer any firm muscle for the ureter to be compressed against as the intravesical pressure increases. Since the lower ureter comes in farther down, it is felt that the bladder is more supportive nearer the trigone and withstands the stress, so that reflux does not occur.

CLINICAL VALUE

Increasing experience with cystography has assessed certain lessons of practical value to the procedure:

A. *Re-evaluation of the child who is not doing well should include cystography.* Of the 26 patients ("old") examined prior to March 1954, by just cystourethroscopy and pyelography, ten (34.4 per cent) showed vesicoureteral reflux. These were all girls. A diagnosis of bladder neck obstruction had been established in nine of the ten and they had been subjected to periodic large caliber urethral dilatations, upwards of 24F. Eight had recurrent symptoms of vesical dysfunction and pyuria, and the degree of reflux demonstrated indicated error in judgment as to initial management. To illustrate: Case 3, K. R., a white girl aged 18 months, was first examined at the age of 4 months (March 1953) for right pyelonephritis. The bladder findings were not considered remarkable, but obstruction from the crossing of the reduplicated ureters was considered as the etiology of the dilated lower pelvis. She was not returned until 14 months later (May 1954), 4 episodes of pyelonephritis having recurred, always preceded by cystitis. Cystography revealed marked reflux to the lower right kidney, establishing the correct diagnosis. See figure 2.

B. *Another lesson learned was the false security of the architecture of the upper tract from excretory urography.* In 14 patients with marked reflux, only three were considered to have abnormal excretory urograms. To illustrate: Case 4, V. L. R., a white girl aged 3 years, had normal excretory urograms but marked bilateral ureteral reflux due to a collarette of the bladder neck. See figure 3.

C. *What had been originally diagnosed as "ureteritis" in the retrograde pyeloureterograms* of case 5, P. M., a white girl aged 2 years, was actually early changes of back pressure from a bladder neck obstruction, and the beginning of

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[8] Hutch, J. A.: Vesicoureteral reflux in the paraplegic: Cause and correction. J. Urol., 68: 457–467, 1952.

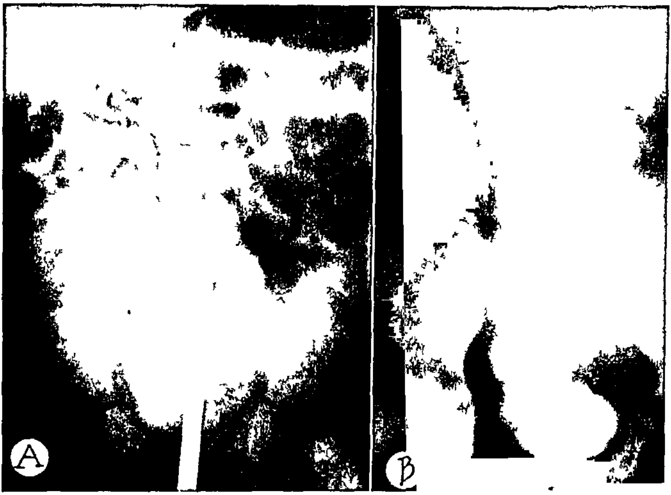

FIG 2 Case 3 *A*, shows retrograde pyeloureterograms with reduplication of right ureters and pelves *B*, post voiding cystogram shows marked vesicoureteral reflux to lower right kidney

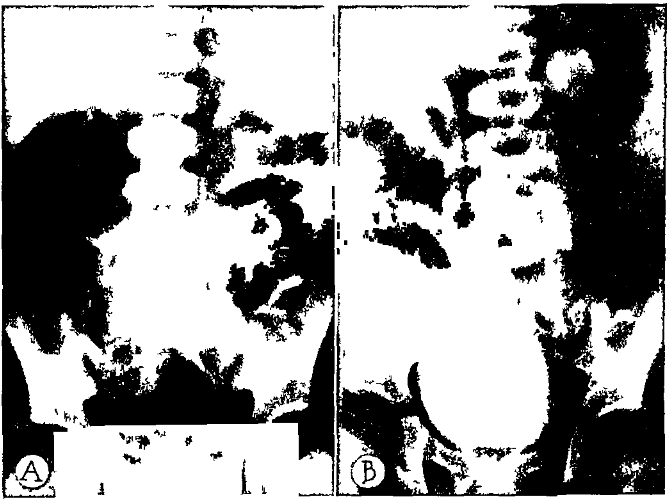

FIG 3 Case 4 *A*, normal excretory urograms *B*, gravity cystogram revealing marked vesicoureteral reflux with ureterectasis

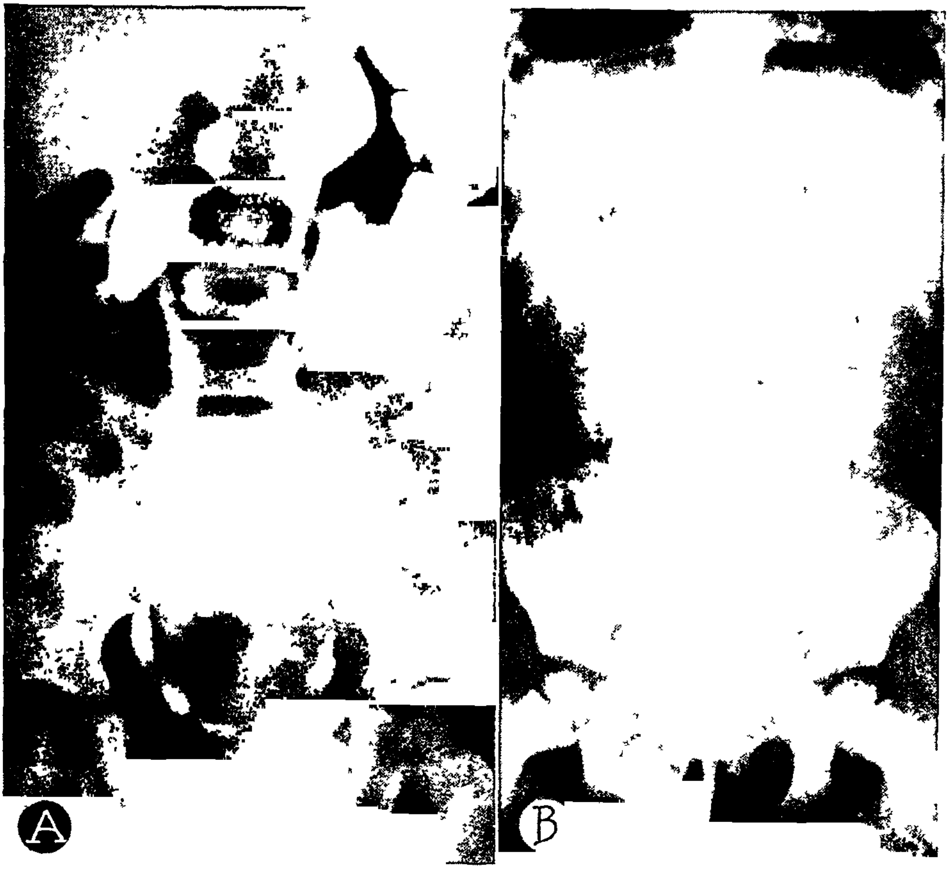

FIG. 4. Case 5. *A*, "rippling of ureters" in retrograde pyeloureterograms. This denotes early changes of back pressure. *B*, gravity cystogram with marked vesicoureteral reflux and tortuous ureters.

the dilated, tortuous ureter. This has been noted in six of 20 patients with reflux, an incidence of 33.3 per cent, and has been designated the *"rippling effect of the ureter"* for want of a better term. When this is noted in the retrograde pyelogram, infravesical obstruction must be strongly considered as cystography will probably show reflux. See figure 4.

D. *Residual urine, where is it?* An explanation for varying residual must consider reflux, for the residual may be in one or both ureters and not in the bladder. Case 6, G. S., a white girl aged 6 years, showed reflux up the lower half of a reduplicated kidney and ureter on the right in the gravity cystogram. This was increased in the immediate post-voiding film although the bladder was emptied. If the patient were catheterized a few minutes after voiding, the ureter would have emptied, and there would obviously be residual urine in the bladder. See figure 5.

E. *The enlarged, thick bladder, plus dilated ureters, minus vesicoureteral reflux,* indicates secondary ureterovesical obstruction. The etiology is hypertrophy of the longitudinal muscles of the ureter secondary to infravesical obstruction accord-

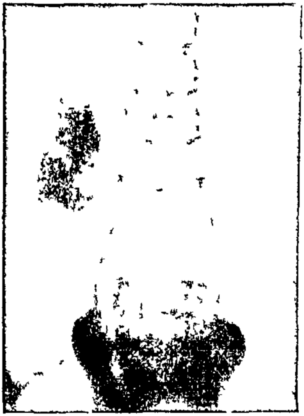

FIG. 5. Case 6. Post voiding cystogram Note empty bladder but marked vesicoureteral reflux

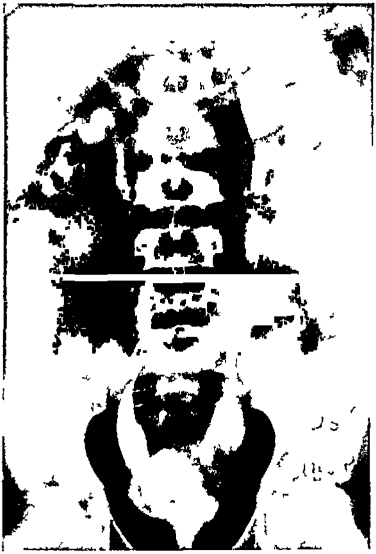

FIG 6 Case 7 Postoperative excretory urogram, 1 month Note return of function Terminal ureters are tapered as they traverse thickened bladder

ing to Kretschmer and Hibbs.[9] To illustrate: Case 7, F. L., aged 10, a white boy, was referred for investigation of long standing diurnal incontinence. Pyuria had been present only 2 weeks. He had 450 cc residual, an enlarged bladder and a diverticulum, but vesicoureteral reflux could not be produced in the gravity, voiding, or delayed cystogram. Excretory urograms revealed poor function and marked dilatation of the upper tract. This was promptly reduced and function improved 1 month after retropubic resection of the bladder neck, diverticulectomy, and suprapubic drainage. Progression of the ureterectasis can be expected to cease, provided the infravesical obstruction is relieved. Obviously ureteral meatotomies would invite reflux and additional infection. See figure 6

DISCUSSION

In a 10-month period, 60 children have been seen with varying degrees of bladder neck obstruction. Concomitant strictures of the external urethral meatus were common. Only one child has been seen with significant ureteropelvic junction obstruction during the same period of time. It is obvious, therefore, that radiographic study of vesical function is of paramount importance. Cystourethroscopy and pyelography alone are inadequate. Burns[10] states that in his experience, retrograde cystography has been the most valuable of all urographic studies of bladder neck obstruction in children.

The diagnosis of significant infravesical obstruction is not always simple. Observation of the voided stream may be misleading as it may be normal in size and force. Repeated checks of residual urine will vary from 0 to 1 or 2 ounces. The use of the foroblique lens must be used to readily detect trabeculation. Fibrosis in the bladder neck will not be fully appreciated until the bladder and posterior urethra are completely distended and the foroblique lens is positioned at the inframontane area. Calibration of the urethra with bulbs completes the instrumental examination.

Whereas, it is desirable to make the proper correction of obstructive uropathy in the child, it is impossible to predict the existing back pressure effects from: 1) cystoscopic appearance of the ureteral orifice, 2) nature of trabeculation, 3) degree of bladder neck obstruction. Excretory urography and retrograde pyelography, likewise, have been misleading. These have also been the observations of Stewart.[11] It is logical, therefore, that cystography be part of the diagnostic team in pediatric urology. The immediate post-voiding cystogram is considered most contributory for the detection of residual urine and serious vesicoureteral reflux. Delayed cystography is a good procedure, but the additional time required (15 minutes versus 2–3 hours) does not compensate for the very occasional case of vesicoureteral reflux missed by voiding cystography.

Treatment may be conservative or operative. Many patients with slight obstruction and minimal findings respond well to dilatation. This is a comparatively recent series (March 1954 to January 1955), and the results of endoscopic versus open surgery are inconclusive to date The Bradford Young[12] procedure or the Bonnin modification[13] is the present method of choice by the authors Vesicoureteroplasty as described by Hutch[8] and Bunge[9] has not been tried on the ureter with reflux It would seem that adequate removal of the infravesical obstruction would take care of the reflux Three postoperative cautions are worthy of mention: 1) close followup of the patient, including periodic urethral dilatations and repeat cystograms, 2) establishment of frequent voidings in the patient with reflux, 3) maintenance of the child on urinary antiseptics for a long period of time

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[11] Stewart, C. M.: Delayed cystography. Bull. Moore-White Med. Found., 5: 49–52, 1954.

SUMMARY

An attempt has been made to show the value of cystography in children Personal experiences with combined gravity and voiding cystography have been presented Vesicoureteral reflux has been demonstrated in 50 per cent more patients after voiding cystography The incidence of reflux was ten in 74 new, consecutive patients (13 5 per cent)

Excretory urograms are misleading as eleven of 14 patients (78 5 per cent) with serious vesicoureteral reflux were considered to have normal pyelograms

The "rippling of the ureter" in the retrograde pyeloureterogram may indicate the effects of reflux, being present in 6 of 20 patients

It is felt that reduplication of the ureter predisposes the upper ureter to incompetency when there is concomitant infravesical obstruction

CONCLUSIONS

Investigation of the pediatric urological problem is incomplete without cystography The additional time required to properly study the patient will be well rewarded by more accurate evaluation of each problem and by the feeling of a job well done

940 Margaret Place, Shreveport, La

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[13] Nesbit, R M and Crenshaw, W B Treatment of bladder neck contracture by plastic operation J Urol, 73 516–519 1955

The Journal of Urology
Vol. 75, No. 1, January 1956
Printed in U.S.A.

ABDOMINAL VENOGRAPHY IN UROLOGICAL DIAGNOSIS

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Although roentgen visualization of the inferior vena cava has a limited sphere of application, it may occasionally provide information of considerable importance in urological diagnosis. Renal and adrenal tumors frequently involve the vena cava by direct venous extension of tumor thrombus or by external compression.[1, 2, 3] Testicular tumors commonly metastasize to retroperitoneal lymph nodes and cause compression or deformity of the inferior vena cava. Anomalies of the vena cava may involve the ureter as in retrocaval ureter. Abdominal venography in such instances may provide information which is unobtainable by other clinical methods.

Development of abdominal venography is relatively new and incomplete. The first description of roentgen visualization of the inferior vena cava was made in 1935 by Dos Santos[4] but only in the last decade have other reports of its use appeared in the literature.[5-10] The methods used for outlining the vena cava have consisted of injection of contrast medium into the veins of the leg or thigh by surgical exposure or percutaneous venipuncture. Our methods are described elsewhere in detail.[11] These involve bilateral, percutaneous femoral vein puncture, translumbar vena cava puncture or percutaneous femoral vein catheterization. Blood pressure cuffs on the thighs and the Valsalva maneuver have been employed to concentrate the contrast medium in the abdominal veins during x-ray exposure.

Figure 1 illustrates anatomical relations of the inferior vena cava. Figure 2 illustrates the major paracaval collateral circulation. The communication of the inferior vena cava with iliolumbar, vertebral and azygos venous systems are abundant. Extensive collateral circulation accounts for the paucity of clinical

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Read at annual meeting, American Urological Association, Los Angeles, Calif. May 19, 1955.

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[4] Dos Santos, R.: Phlebographie d'une Veine Cava Inferieure Sutures. J. d'urol., **39:** 586–587, 1935.

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[11] Kaufman, J. J. and Burke, D. E.: Abdominal venography: Methods of roentgen visualization of the inferior vena cava. To be published, Am. J. Roentgen.

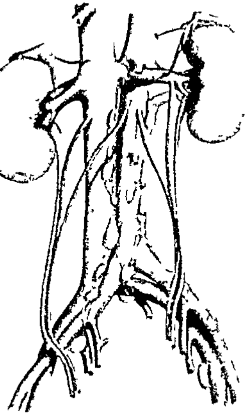

Fig. 1. Anatomical relations of the inferior vena cava

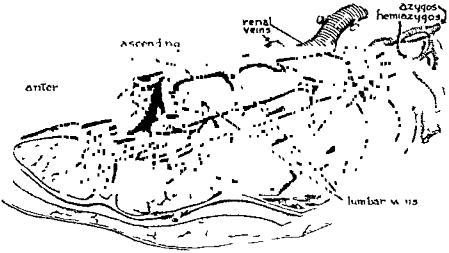

Fig. 2. Artist's drawing of major paracaval collateral channels

signs and symptoms when the inferior vena cava is partially or completely occluded below the renal veins.[12, 13] Figure 3 is a normal vena cavagram obtained by injection of 25 cc of urokon 70 per cent simultaneously in each femoral vein. The abdominal vena cava is outlined in its entirety. Slight reflux into the internal iliac veins is commonly seen during the Valsalva effort.

CASE REPORTS

Case 1. R.M. (GH 36531), a 60-year-old white man, had a right nephrectomy for hypernephroma in January 1953. At the time of surgery there was no evidence of distant metastases or local extension of the renal tumor. However, tumor thrombus was found in the renal veins on gross examination of the resected

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[12] Wakefield, E. G. and Mayo, C. W : Obstruction of the vena cava distal to the renal veins J. Missouri M.A., 31: 92–96, 1934

[13] Keen, J A.: Collateral venous circulation in a case of thrombosis of the inferior vena cava and its embryological interpretation. Brit. J. Surg., 29: 105–108, 1941.

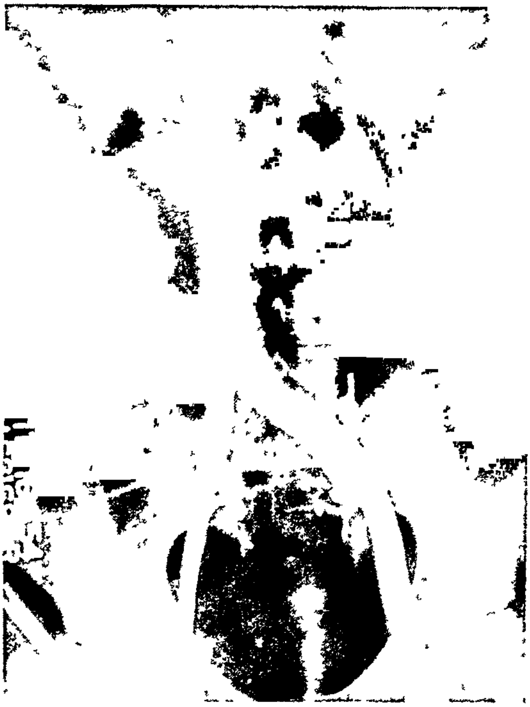

Fig. 3. Normal vena cavagram obtained by bilateral femoral venipuncture percutaneously

specimen. The patient did well postoperatively for a period of 8 months but then began to experience deep abdominal pain and mild pain and edema in both lower extremities. There was no weight loss, and x-ray examination of the chest disclosed no metastases. Excretory urography revealed a normal functioning left kidney. Reoperation for a "second look" was considered until vena cavagram, done in September 1953 by percutaneous puncture of the femoral veins, revealed a large filling defect of the upper abdominal vena cava suggestive of tumor thrombus (fig. 4, *A*). Pulmonary metastases subsequently developed and the patient died. At autopsy, 3 months following the vena cavagram, a large malignant tumor thrombus was found extending from the vena cava to the right auricle.

Case 2. R.H. (GH 51680), a 33-year-old white man, entered the hospital complaining of hematuria and left upper quadrant mass. A retrograde pyelogram on February 24, 1955 disclosed a bizarre deformity of the pelvis and calyces with displacement and compression by a mass in the medial portion of the kidney. The clinical diagnosis was renal tumor. Translumbar aortography showed no pooling of dye. Vena cavagram revealed lateral displacement of the midportion of the inferior vena cava with notching of the medial border suggestive of external node compression (fig. 4, *B*). A large Wilms' tumor of the left kidney was removed thoracoabdominally. Numerous pericaval metastatic lymph nodes were found. Because of the extent of involvement no node dissection was attempted.

Case 3. S.S. (GH 48734), a 54-year-old white man, had a left nephrectomy in September 1954 for hypernephroid carcinoma. Renal vein involvement by tumor thrombus was noted in the specimen. The patient re-entered the hospital 4

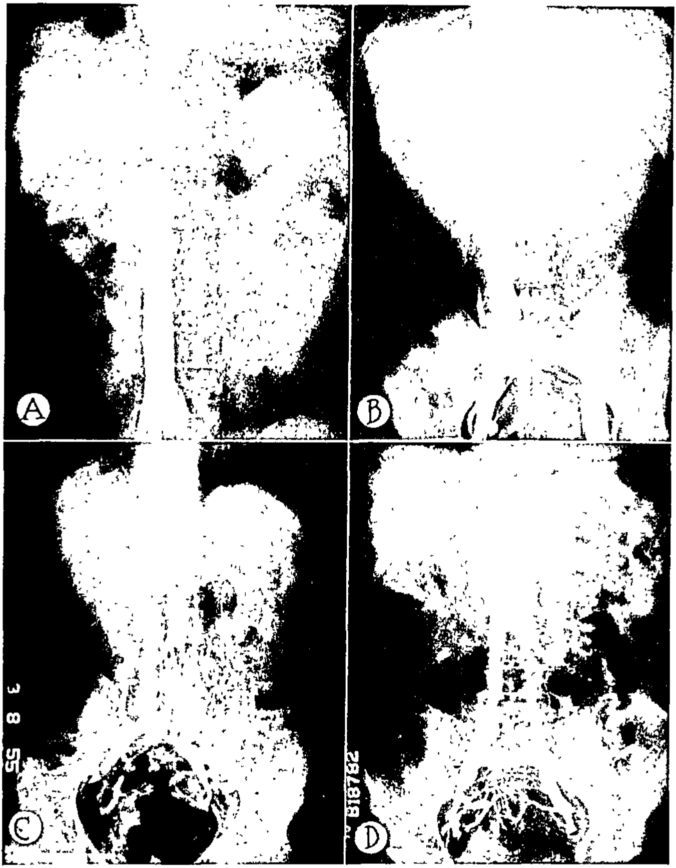

Fig. 4. *A*, vena cavagram showing large filling defect caused by intraluminal tumor extension from hypernephroma, right kidney. *B*, vena cavagram showing lateral displacement of the vena cava with notching of the medial border suggestive of external node compression. *C*, vena cavagram showing subtotal block by tumor thrombus. Extensive collateral venous channels are seen. *D*, vena cavagram showing filling defect secondary to tumor thrombus (hypernephroma). Presacral collateral circulation is evidence of partial caval block.

months later complaining of abdominal pain. There was no evidence of ascites, leg swelling or dilated superficial abdominal veins. A vena cavagram showed a subtotal block of the inferior vena cava by tumor thrombus with extensive collateral venous channels, i.e., ascending lumbar and vertebral veins (fig. 4. *C*).

Case 4. E. O. (GH 51924), a 55-year-old white man, was admitted to the hospital because of gross hematuria. Retrograde pyelography disclosed a large

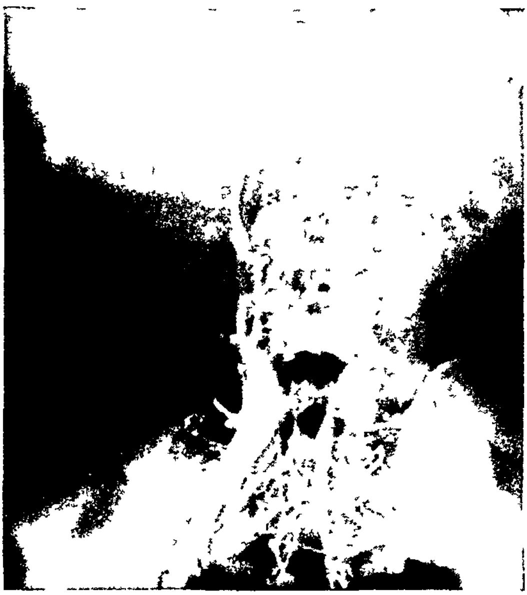

Fig. 5. Scalloping of inferior vena cava secondary to external node compression. Metastatic testis tumor.

tumor of the left kidney deforming and attenuating the calyces. Aortography revealed laking of dye suggestive of hypernephroid carcinoma. The left kidney was removed on March 25, 1955 through a lumbar incision. At the time of surgery tumor thrombus was found in the renal vein, and extension of renal tumor into the inferior vena cava above the left renal vein was suspected although not confirmed. Two weeks postoperatively vena cavagram was performed by catheterizing the right femoral vein percutaneously. Figure 4, *D* shows a filling defect in the inferior vena cava compatible with tumor thrombus. It also demonstrates presacral, collateral, anastomotic channels indicative of partial occlusion of the vena cava.

Case 5. E.R. (GH 47854), 24-year-old Mexican man, sustained trauma to the right testis in 1951. Two years later an enlarged testis was noted on routine examination and surgery was advised. In May 1954 simple right orchiectomy was performed at another hospital and revealed embryonal carcinoma. The patient was referred to this hospital for x-ray therapy. On July 8, 1954 x-ray examination of the chest suggested hilar node enlargement. Presacral oxygen insufflation was done and no ascent of gas was noted on the right side. On July 15, 1954 abdominal venography was performed by percutaneous injection of the right femoral vein (fig. 5). The roentgenogram clearly shows scalloping of the vena cava secondary to extrinsic node compression. Extensive collateral circulation through the arcaded vertebral plexus is evidence of partial occlusion of the vena cava. One month later a chest film revealed multiple pulmonary metastases. The patient died outside the hospital on October 7, 1954. No autopsy was obtained.

Case 6. J.R. (GH 11312), a 35-year-old white man, had a right orchiectomy in 1949 for seminoma. He was treated with radiation therapy to the retroperitoneal area and to the mediastinum postoperatively. He did well for 4½ years. Then

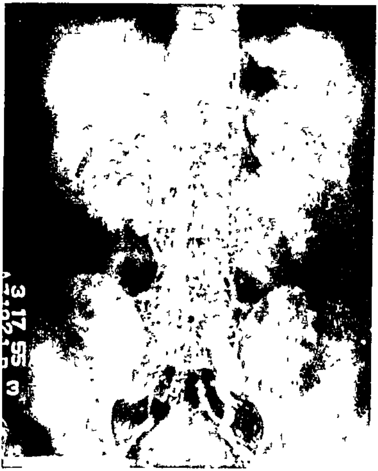

Fig. 6. Complete block of inferior vena cava secondary to metastatic nodes from seminoma of testis.

he began to have pain in the right flank and right lower quadrant. On admission there was no evidence of chest metastases. Excretory urography revealed mild right hydronephrosis with medial deviation of the mid-ureter suggestive of extrinsic pressure. On March 17, 1955 an abdominal venogram was done by bilateral percutaneous femoral venipuncture. No ascent of dye was seen in the vena cava, and extensive collateral circulation through the vertebral plexus and ascending lumbar system confirmed the complete block of the vena cava (fig. 6). On March 28, 1955 surgical exploration corroborated the radiographic findings of inoperable retroperitoneal lymph node metastases. The patient was given additional radiation therapy.

DISCUSSION

In 1911 Pleasants[14] collected 314 cases of obstruction of the inferior vena cava. Fifty of these (16 per cent) were due to neoplastic invasion. In 1924 Simpson[15] added 28 cases of inferior vena cava obstruction by direct tumor invasion. Fifty per cent of tumor invasions of the inferior vena cava were secondary to renal neoplasms. In respect to this it has been estimated that 23 per cent of renal tumors invade the renal veins.[16] Twenty per cent of the cases of caval obstruction were due to involvement by testis tumors in the form of extrinsic node compression or by direct invasion of the wall of the vena cava. Adrenal tumors accounted for 9 per cent of the caval obstructions and were due entirely to direct growth through the suprarenal veins into the vena cava. Retroperitoneal sarcomas and tumors of the liver, pelvic bones, stomach, uterus, ovary and pancreas accounted for the remainder of malignant tumor obstructions of the inferior vena cava.

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[14] Pleasants, J. H : Obstruction of inferior vena cava with a report of 18 cases. Johns Hopkins Hosp Rep., 16: 363–548, 1911.

[15] Simpson, W. E.: Tumor thrombus of the inferior vena cava. Ann. Clin. Med., 3: 29–86, 1924.

[16] Mellins, H Z.· Functions of the vertebral venous circulation. Bull. U Minn. Med. Found , 22: 213–224, 1951

It has been emphasized repeatedly that the clinical picture associated with inferior vena cava obstruction is usually mild.[17, 18] In 50 per cent of reported cases there were no clinical symptoms suggestive of caval obstruction. It is now well known that ligation of the inferior vena cava below the renal veins is well tolerated and is frequently unassociated with the development of signs or symptoms such as leg edema.[18] The absence of signs of inferior vena cava obstruction is due to the deep collateral venous system consisting of the vertebral veins, ilio-lumbar and ascending lumbar veins communicating with the azygos and hemi-azygos systems. There are rich anastomoses occurring segmentally which connect the lumbar veins to the vertebral venous plexus. These collateral veins can apparently operate adequately to drain the venous return of the pelvis and lower extremities even when the inferior vena cava is suddenly occluded. This explains why ascites, dilated superficial abdominal veins and persistent leg edema are not more frequent sequelae of inferior vena cava block. When the iliac veins are involved by thrombosis or compression, leg edema is more common since effective collateral circulation stems largely from the iliacs.

Obstruction of the middle third of the vena cava at the level of the renal veins is not well tolerated unless adequate collateral venous return from the kidneys has been developed. Lespinasse[19] showed experimentally that the vena cava can be ligated above both renal veins with relative impunity provided that preliminary ligation of the vena cava is done below the renal veins and that time is then allowed for collateral channels to open. Ripstein and Miller[20] recently reported a case of almost complete sudden occlusion of the inferior vena cava above the renal veins. Passive congestion of the kidneys led to renal failure and uremia. The use of the artificial kidney allowed time for development of collateral venous return. When this occurred, renal function was restored and the patient recovered. These reports suggest that the vertebral venous plexus and the ascending lumbar and azygos systems are sufficient to maintain venous drainage from the kidneys—particularly if caval ligation below the renal veins is done to decrease the burden on the collateral venous system draining the kidneys. Occlusion of the upper third of the inferior vena cava often produces a dramatic clinical picture (Budd-Chiari syndrome). If the hepatic vein or its ostium is involved, enlargement of the liver and spleen with ascites and jaundice often develops.

The demonstration of caval disease by abdominal venography may seriously alter the treatment and prognosis. Scholl and Judd[1] stated that extension of

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[18] O'Neil, E. E.: Ligation of the inferior vena cava in the prevention and treatment of pulmonary embolism. New Eng. J. Med., **232:** 641–644, 1945.

[19] Lespinasse, V.: Ligation of the vena cava above the renal veins with and without nephrectomy. Quart. Bull. Northwestern Univ. Med. Sch., **21:** 312, 1947.

[20] Ripstein, C. B. and Miller, C. G.: Obstruction of the inferior vena cava above the renal veins. Ann. Surg., **130:** 958, 1949.

tumors into the renal veins and vena cava greatly increases both immediate and late mortality statistics in which nephrectomy is performed for malignancy They showed that when the renal vein is involved only 11 per cent of patients have a life expectancy of from 3 to 14 years Dean[21] emphasizes that results of nephrectomy for carcinoma indicate that most operations are not sufficiently radical He advises removal of all perirenal fat and a clean dissection of nodes and lymphatics about the great vessels up to the diaphragm He also states that opening of the inferior vena cava to remove a tumor thrombus may be necessary Belt[22] reports an instance where a patient lived over 12 years without evidence of tumor recurrence following nephrectomy for carcinoma extending into the vena cava and where a large tumor thrombus was removed from the cava through the opened renal vein Other urologists feel that such attempts to remove tumor thrombus from the vena cava are futile gestures, but agree that removal of a segment of inferior vena cava below the renal veins may aid *en bloc* excision of a large tumor adherent to the vena cava[23, 24, 25] Removal of part of the wall of the inferior vena cava where the tumor is attached, along with the renal vein and kidney *on that side may at times be indicated Such radical surgery* can be made more feasible by preoperative knowledge of the presence of intracaval extension of tumor thrombi or of caval fixation by tumor For this reason abdominal venography should be part of the preoperative investigation of any patient with an advanced renal tumor

Demonstration of gross deformity and compression of the inferior vena cava by retroperitoneal lymph node metastases from testis tumors can preclude the feasibility of radical retroperitoneal node dissection In these cases reliance must be placed on radiation therapy alone However, a normal vena cavagram in a case of testicular neoplasm does not exclude metastatic disease of retroperitoneal lymph nodes In our series we have not demonstrated retroperitoneal lymph node metastases from carcinomas of the bladder or prostate However, it is well known that such tumors frequently metastasize to retroperitoneal lymph nodes Abdominal venography may occasionally demonstrate such conditions when the clinical diagnosis of metastatic disease is obscure

We feel that the indications for abdominal venography are as follows

1) To confirm suspected caval obstruction when there are ascites, dilated superficial veins and leg or scrotal edema

2) To ascertain the presence of caval disease when there are no clinical signs or symptoms to suggest obstruction (renal, testicular, adrenal and possibly bladder and prostatic cancers)

3) To detect tumor thrombus formation in the vena cava when advanced renal and adrenal neoplasms are known to exist

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[21] Dean A L The surgical treatment of tumors of the genito urinary organs J Urol , 70 246 256 1953

[22] Belt L Personal communication

[23] Foley, F E B , Mulvaney, W P , Richardson, E J and Victor, I Radical nephrectomy for neoplasm J Urol , 68 39–49, 1952

[24] Marshall V F and Schmidlapp, C J Partial excision of the inferior vena cava in the removal of tumors Cancer, 2 316, 1949

[25] Donovan H A Malignant right kidney removed at operation together with a short length of vena cava Brit J Urol , 17 107, 1945

4) To demonstrate the course of the vena cava in relation to the ureter when retrocaval ureter is suspected.

5) To aid in diagnosis of retroperitoneal tumors such as lymphomas or metastatic tumors when the primary source is unknown.

6) To localize retroperitoneal tumors, primary or metastatic, in order to plan x-ray therapy.

We have performed vena cavagrams in 50 patients and except for transient discomfort associated with extravasation of dye outside the femoral vein in approximately 20 per cent of cases we have seen no untoward effects resulting from its use. The procedure is as safe as intravenous urography. The contraindications to abdominal venography are sensitivity to the organic iodide preparations and the presence of active thrombophlebitis of leg or pelvic veins. We feel that the dangers of dislodging tumor thrombi from the inferior vena cava are negligible since insufficient pressure is created in this distensible organ.

SUMMARY

Urologists have not yet generally availed themselves of abdominal venography to aid in diagnosis of genitourinary tumors and their spread.

Roentgen visualization of the inferior vena cava is a relatively simple diagnostic procedure. It can be performed by bilateral femoral venipuncture, translumbar caval puncture or percutaneous femoral vein catheterization. Femoral venipuncture is the simplest and can be performed on the ambulatory patient.

We have used caval phlebography to demonstrate invasion and compression of the inferior vena cava by renal and testicular neoplasms, and to aid in the diagnosis of retrocaval ureter.

Complete obstruction of the inferior vena cava below the level of the renal veins is well tolerated. Often it produces only minimal symptoms owing to the rich, deep, collateral venous return.

True radical surgery for renal tumors may occasionally necessitate removal of a segment of vena cava or extraction of caval tumor thrombi. Preoperative vena cavagrams may provide information which will be helpful in planning radical surgery.

The demonstration of retroperitoneal metastasis from genitourinary tumors by abdominal venography may seriously alter prognosis and may preclude operability.

A vena cavagram is useful in confirming the diagnosis of retrocaval ureter.

CONCLUSIONS

In conclusion, we believe that abdominal venography deserves further use among urologists. Although indications for caval phlebography are not common and the method will never become widespread, it is a useful procedure in selected cases and may yield valuable information where the diagnosis of caval disease is otherwise unobtainable by clinical means. It is a simple procedure without significant risk. The information derived may be of importance in determining the method of treating tumors of the kidney, adrenal and testis; and in the study of these tumors, abdominal venography fills a definite need in our diagnostic resources.

THE JOURNAL OF UROLOGY
Vol. 75, No. 1, January 1956
Printed in U.S.A.

NEW TECHNIQUE OF TRANSLUMBAR AORTIC CATHETERIZATION

JORGE CUÉLLAR

After doing aortographies for some time with a regular No. 18 aortography needle, I thought that if I could use a larger special needle with a wider interior diameter, I could pass a catheter through it to any level in the aorta and maybe even to the renal artery.

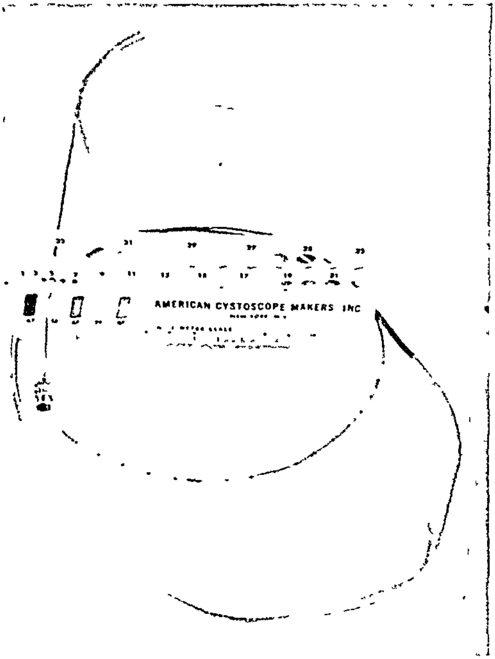

FIG. 1

I considered the procedure safe after knowing the works of Euler and Wickbom, some of which were published in the *Acta Radiologica*, Stockholm, November 1952, where Euler evaluated the relationship between needle caliber and hematoma formation.

Based on this, I designed a silver trocar with an external diameter of 1.7 mm. that allowed a German Cournand No. 4 catheter through its interior. The stylet used was a regular No. 18 aortography needle (fig. 1).

Read at annual meeting, Southeastern Section of American Urological Association, New Orleans, La. March 20-24, 1955

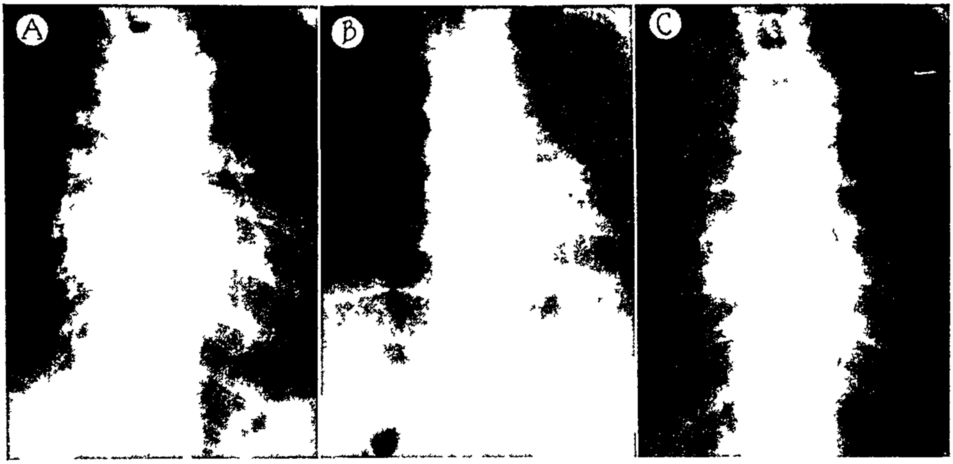

FIG. 2

The technique is the same one as for a regular aortography. However, I have always done the puncture with local anesthesia. After having punctured the aorta, the No. 18 needle is removed, leaving the special needle intubating the aorta. The catheter is introduced through the lumen of the needle to any level in the aorta (fig. 2). I found that the catheter usually goes in the left ventricle of the heart if one continues pushing on it (fig. 3). This enables the cardiologist to obtain intraventricular pressures and do other investigations of value within the heart in the diagnosis of cardiac disease. The procedure so far in 15 cases has been harmless.

The principal idea that I had in mind when I developed this method of catheterizing the aorta was to reach a renal artery and thus be able to make selective nephrograms and do other studies in the kidney. However, a new simple way of catheterizing the left ventricle was obtained.

But, even if so far I have not been able to develop a technique of catheterization of the renal arteries, I have not hesitated to bring my paper before this association in the hope that somebody might develop the technique and thus

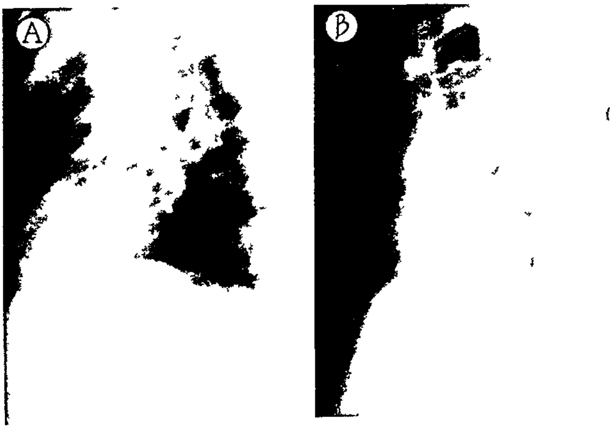

FIG 3

be able to obtain selective nephrograms and do experimental work putting another catheter in the renal vein and a ureteral catheter up the ureter.

Only once after several trials at puncturing the aorta at the level of the renal arteries was I able to puncture the renal artery itself and thus obtain a selective nephrogram (fig. 4).

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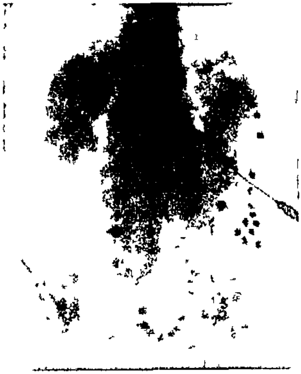

FIG. 4

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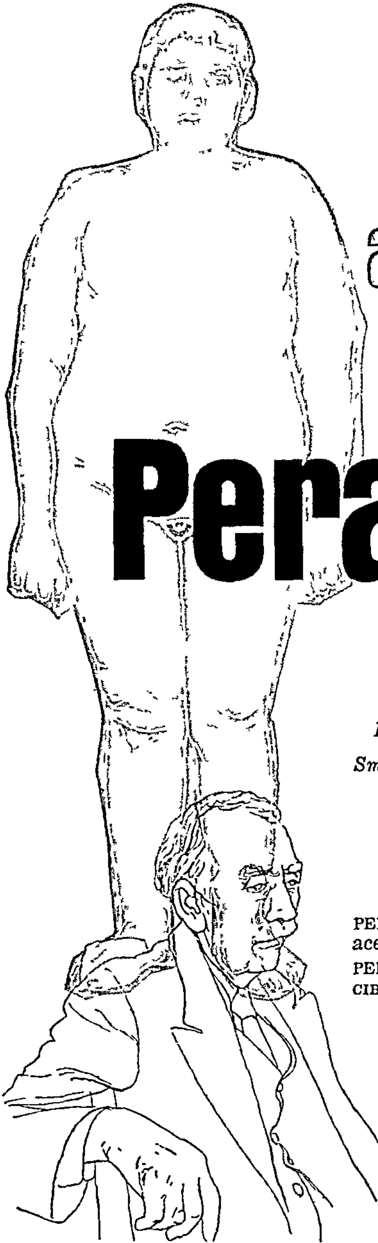
North Central—Cleveland, Ohio, October 3–5, 1956
South Central—Mexico City, dates to be announced later
Southeastern—Hollywood Beach, Fla., March 25–29, 1956
Western—Sheraton-Plaza, San Francisco, April 30–May 3, 1956

Note by editor. A complete list of the executive committees of the various sections, and a complete list of the officers and members of the executive committees of the various branch societies was printed in the December 1955 issue.



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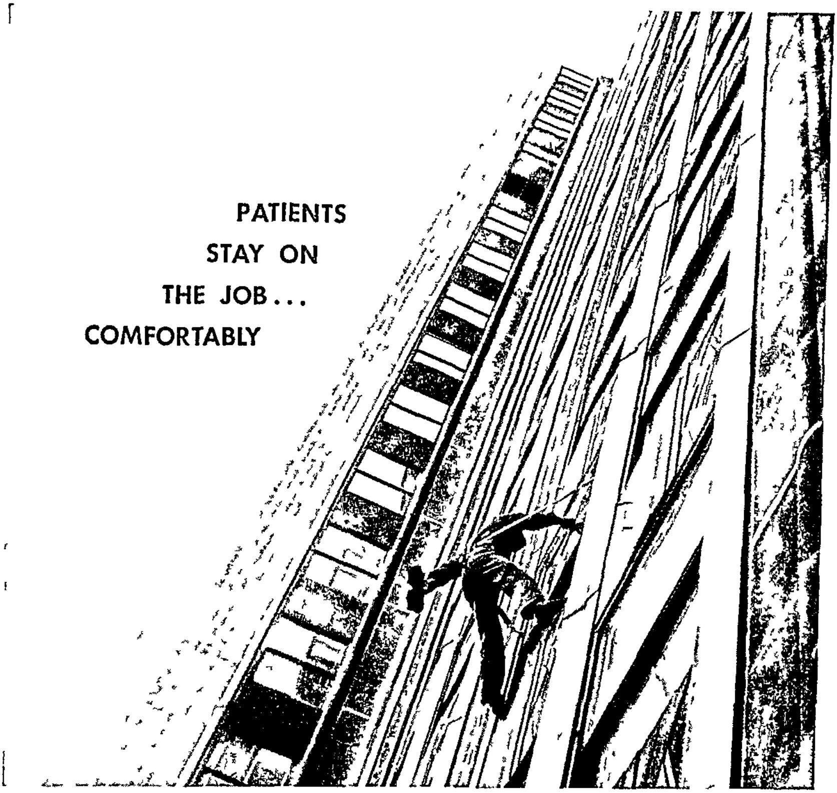

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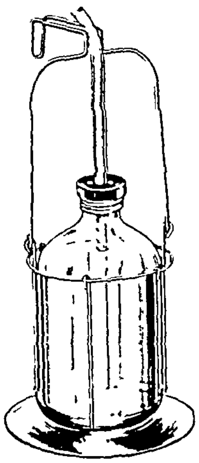

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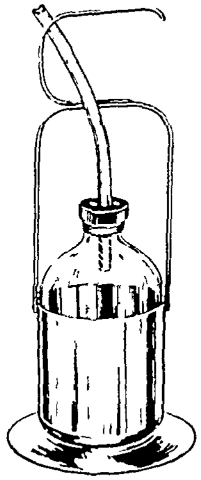

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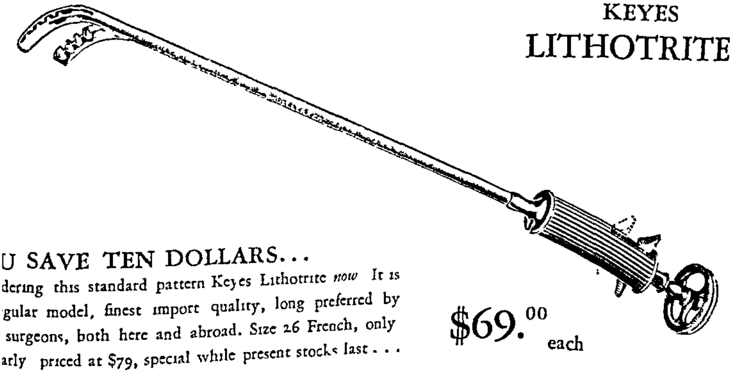

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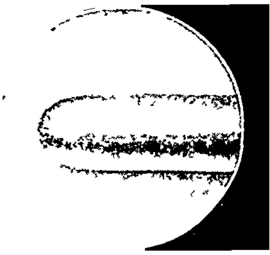

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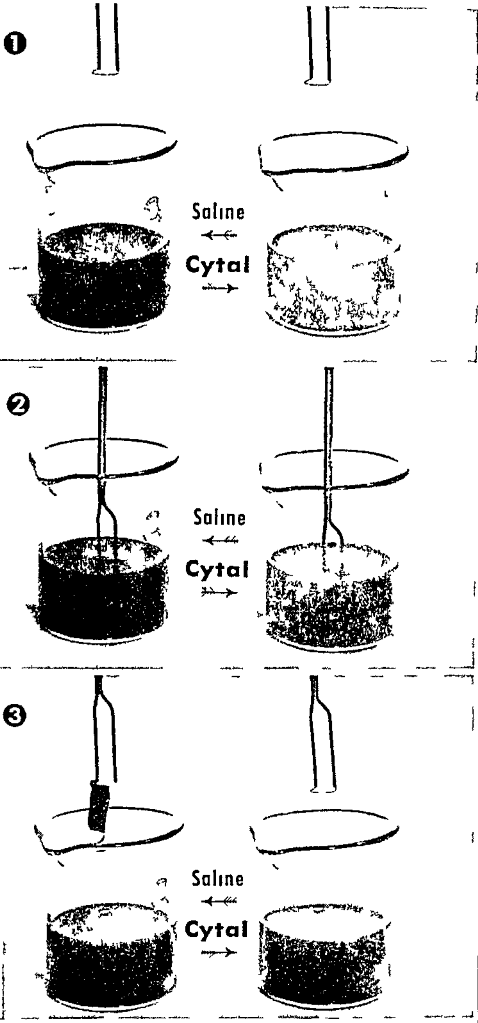

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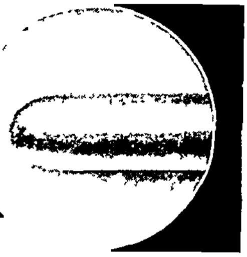

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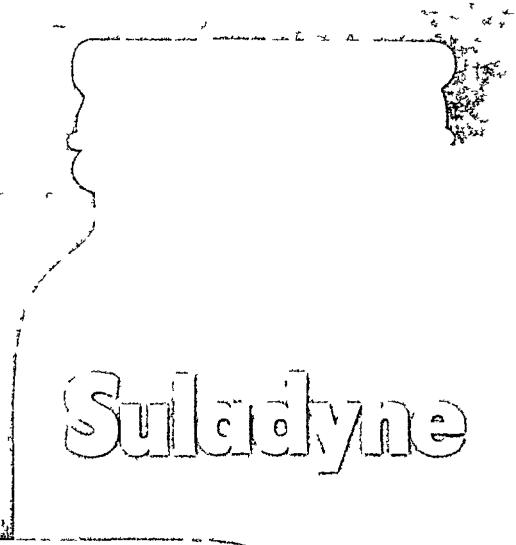

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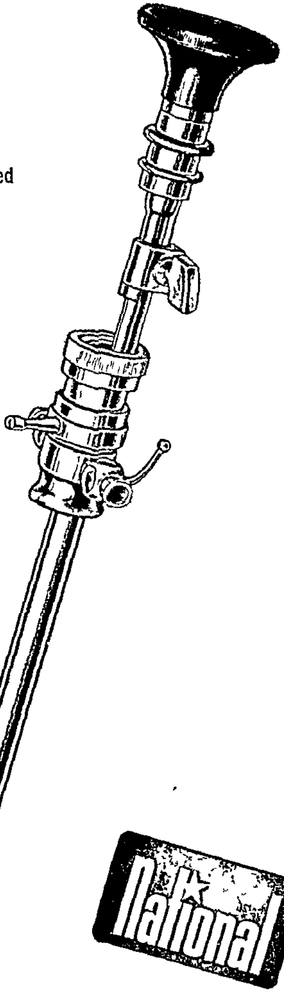

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CONTENTS

Congenital Urinary Tract Obstructions in Children *T R Fetter and K C Warren* 173
Mechanisms of Hydronephrosis *Lester Persky, F J Bonte and George Austen, Jr* 190
Perinephric Abscess Producing a Pneumonephrogram *Robert Braman and R R Cross, Jr* 194
A Low Lying Left Kidney *R E McClellan* 198
Intrinsic Renal Function *J G Edwards* 200
Effect of Temperature, Humidity and Dehydration on Formation of Renal Calculi *C L Prince, P L Scardino and C T Wolan* 209
Influence of Diet on Urinary Citrate Excretion *C L Yarbro* 216
True Prolapse of Ureter *Michael Greenfield* 223
Relief of Upper Ureteral Obstruction within Bifurcation of Renal Artery *N S R Maluf* 229
Metastatic Carcinoma of Ureter *J J Robbins and Robert Lich, Jr* 242
Electropotential Changes in Normal Human Ureter *E L Corey, E H Fite, Jr and S A Vest* 244
Electrourogram, II Experimental Study *A W Kneucker* 250
Cystitis Emphysematosa *J W Lane and Paul Francke* 256
Management of Hunner's Ulcer by Differential Sacral Neurotomy *M K Moulder and A M Meirowsky* 261
Radiographic Estimation of Residual Urine in Children *B W Young, W L Anderson and G G King* 263
Studies of Urinary Incontinence in Men *F A Beneventi and V F Marshall* 273
Testicular Dysgenesis in Relation to Neoplasm of Testicle *A R Sohval* 285
Use of Scrotal Skin to Cover Wound Defects in Groin and Pubic Area *J S Arconti and W E Goodwin* 292
Intrascrotal Adenomatoid Tumor *Charlotte Curtiss and Ernest Hock* 297
Anastomosis of Vas Deferens Experimental Study *S S Schmidt* 300
Prophylactic Use of Chloramphenicol in Transurethral Prostatic Resections *D M Appleton and B A Waisbren* 304
Prostatic Adenocarcinoma Complicated by Development of Epidermoid Carcinoma of Urethra *M J Williams and E I Klein* 314
Lipids in Prostate Gland of Dog *A R Seaman* 324

(*Contents continued on page 38*)

Annual Meeting, American Urological Association, Statler Hotel
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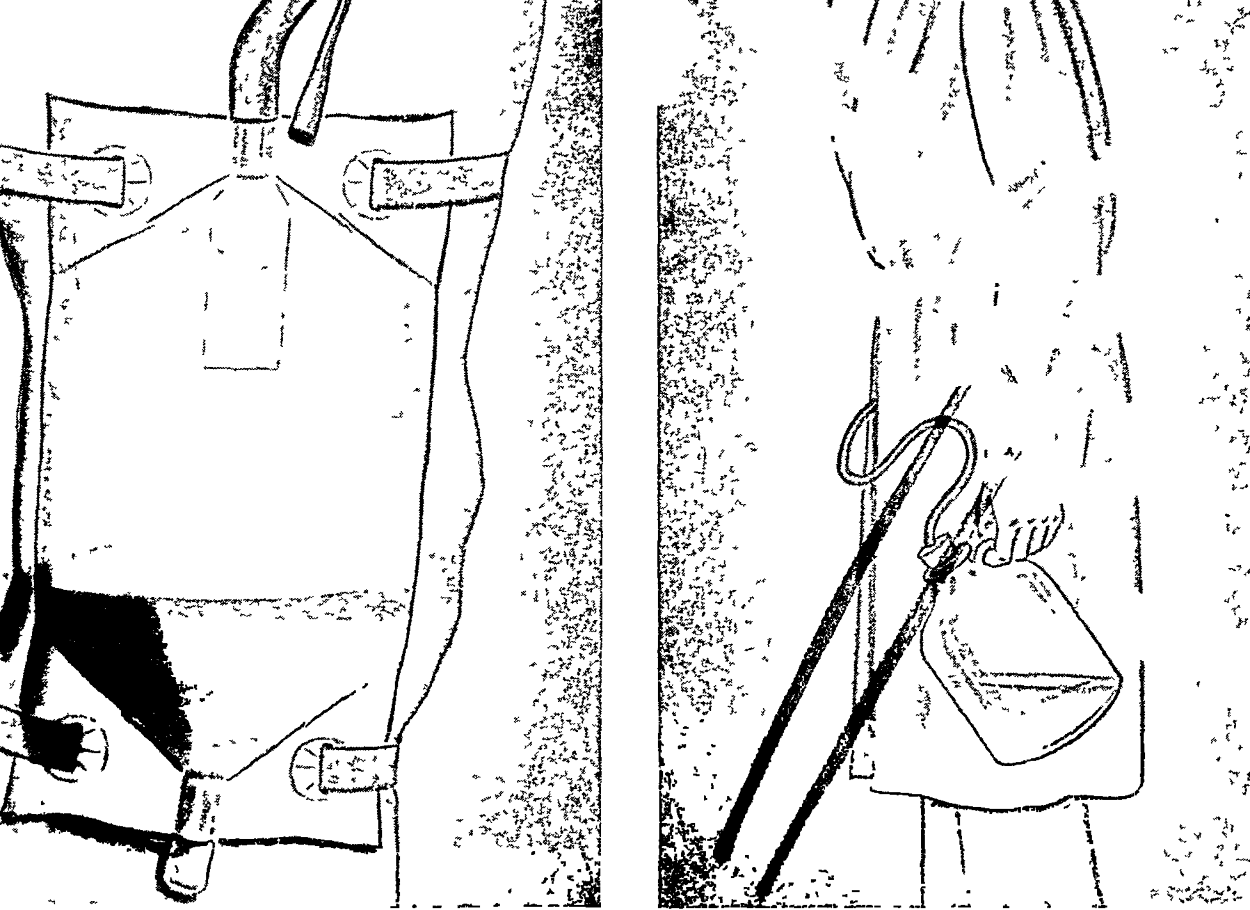

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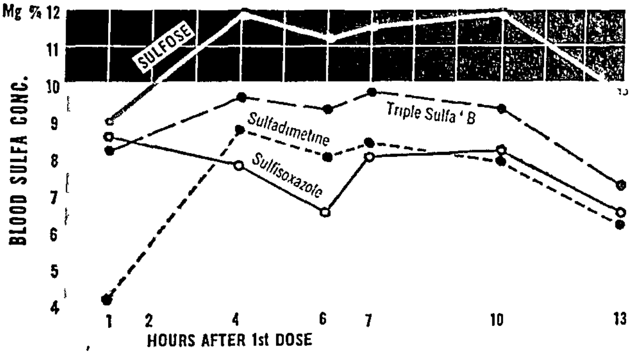

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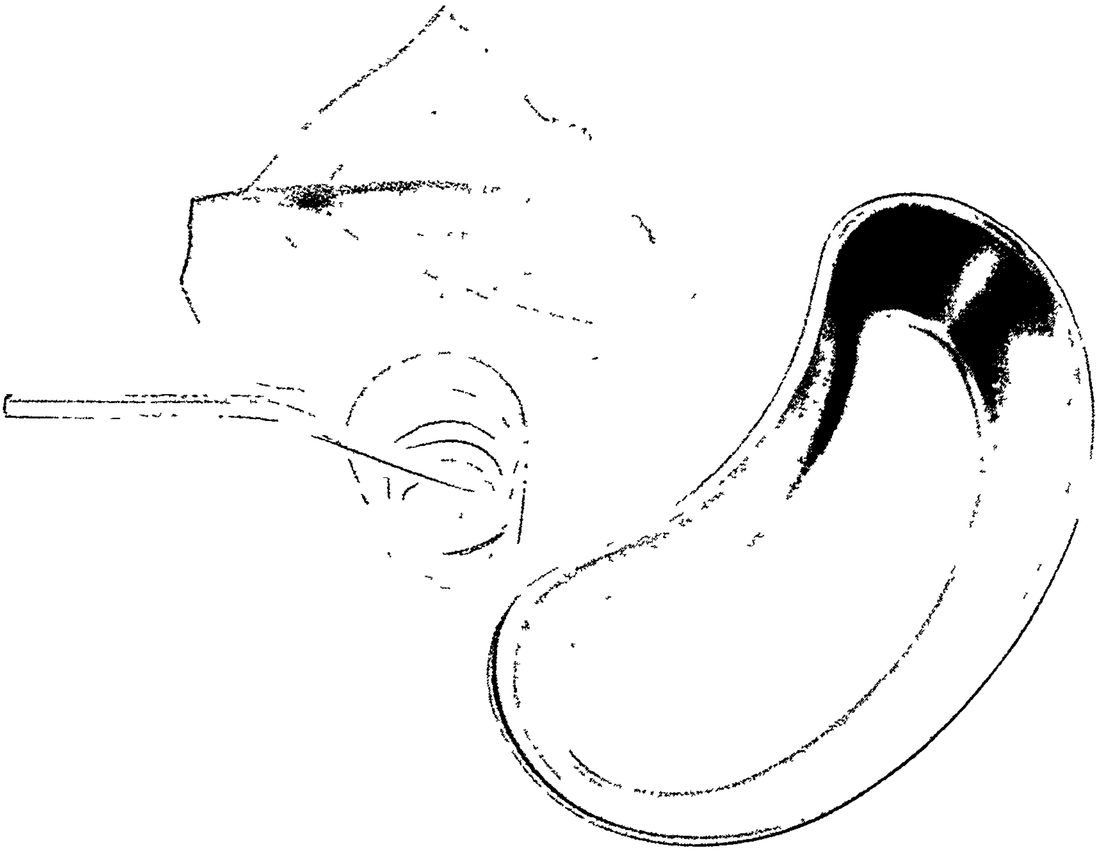

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With 'Thorazine' "postoperative retching seldom is a problem. Intractable nausea and retching due to spinal anesthetics responded . . . Retching caused by organ manipulation also responded."[1]

'Thorazine' administered before general anesthesia "reduced the postoperative vomiting from 28.8 per cent to 13 per cent."[2]

1. Mathews et al Am Pract & Dig Treat 6 360 (Mar.) 1955.
2 Albert and Coakley Anesth & Analg 33.285 (July-Aug.) 1955.

'Thorazine' is available in ampuls, tablets and syrup, as the hydrochloride; and in suppositories, as the base.

'Thorazine' should be administered discriminately; and, before prescribing, the physician should be fully conversant with the available literature.

Smith, Kline & French Laboratories, 1530 Spring Garden Street, Philadelphia 1

**T.M. Reg. U.S. Pat. Off. for chlorpromazine, S.K.F.*

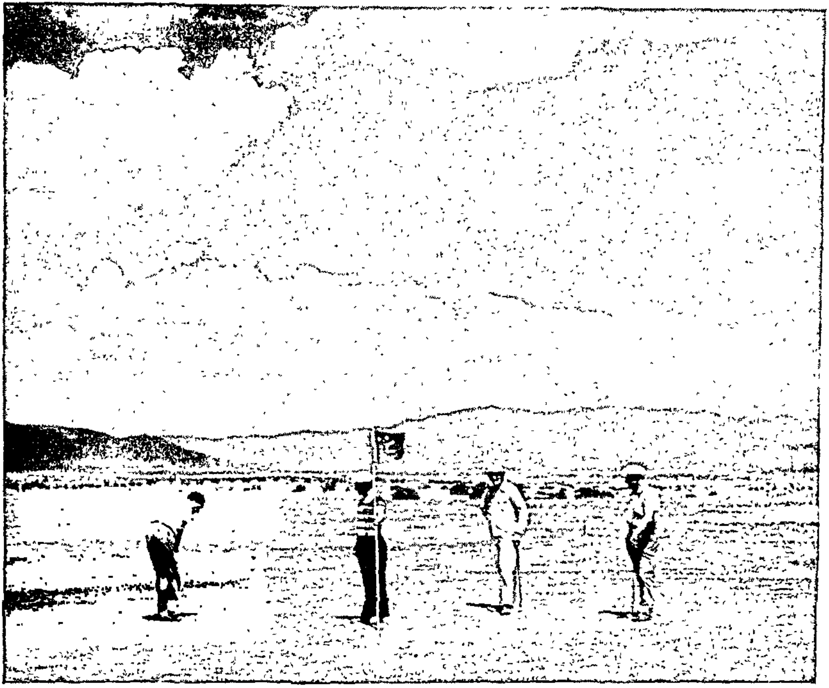
(In writing to advertisers, please mention the journal—it helps.)

Depropanex®

DEPROTEINATED PANCREATIC EXTRACT

promptly relieves spasm and gets him back in the game

MAJOR ADVANTAGES: Relieves spasm in 3 minutes.[1] Acts directly on smooth muscle. Non-narcotic. Nontoxic.



DEPROPANEX dramatically relieves pain of ureteral and renal colic. "There can be no question . . . of the beneficial effect of the drug in lessening or abolishing pain."[2] Useful, too, in biliary colic.

Within three minutes, DEPROPANEX relieves spasm—not by dulling the senses, but by direct action on the smooth muscle. It is therefore especially valuable after cystoscopy and other urologic procedures. In abdominal surgery, DEPROPANEX makes possible an "easier, more pain-free recovery."[3]

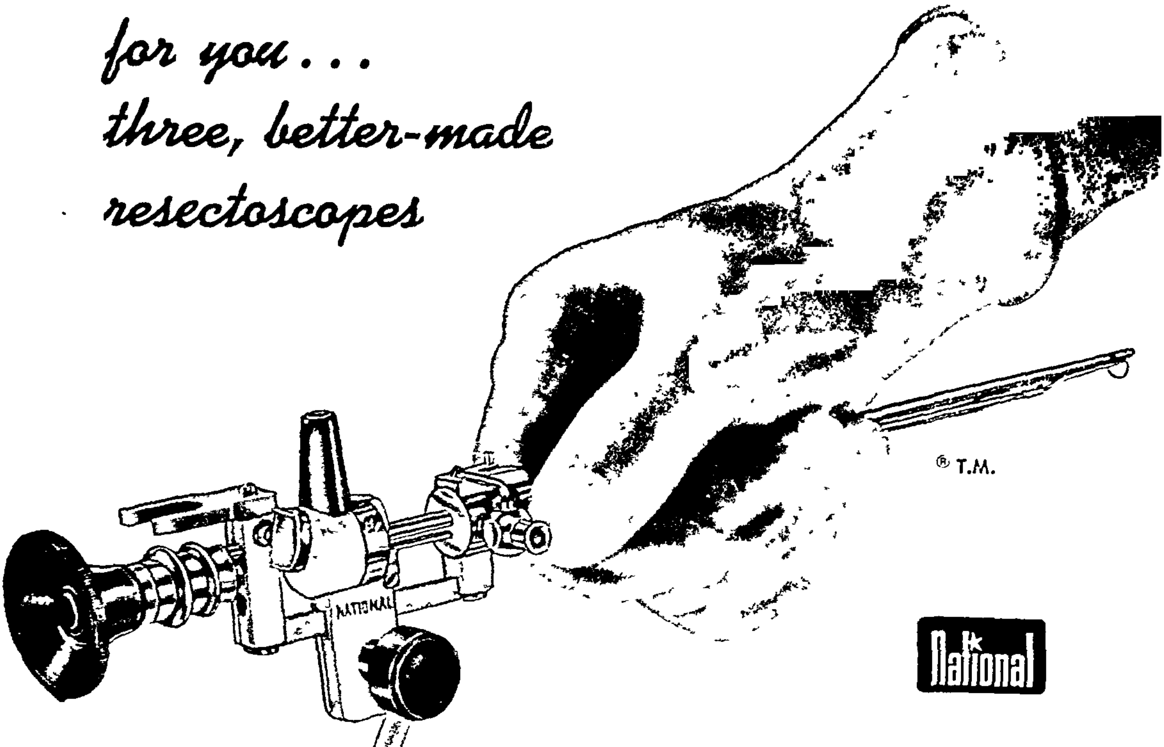
Supplied: 10-cc. and 30-cc. rubber-capped vials. Dosage schedules in package circular.

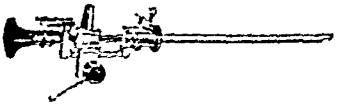
REFERENCES: 1. South.M. J. 31:233, 1938. 2. J. Urol. 51:137, 1944. 3. Minnesota Med. 33:103, 1950.

SHARP & DOHME

Philadelphia 1, Pa.
DIVISION OF MERCK & CO., INC.

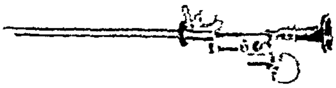
for you . . .
three, better-made
resectoscopes





7152B. Rack and Pinion type

7151B. Flat leaf spring type



7150B. Coiled spring type

Craftsmen have designed and built these three new resectoscopes to give you these three all important features: ***easy manipulation, precision-smooth action and utmost reliability.***

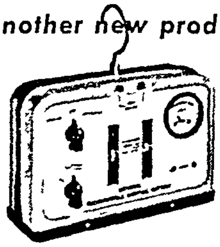
All are of the multiple type with 24, 26 and 28 fr. sheaths. And for your convenience, loops, sheaths, telescope, rotating contact, bulb and working element are *all* interchangeable with corresponding components of other manufacture.

The separately listed National Fontar® Forward Oblique Telescope 6301B for these instruments is also an example of fine craftsmanship. It provides you with a field of vision that is exceptionally bright, clear and wider than you have heretofore known.

★ All priced to provide you savings too ★

Details on any or all these items will be gladly sent you on request.

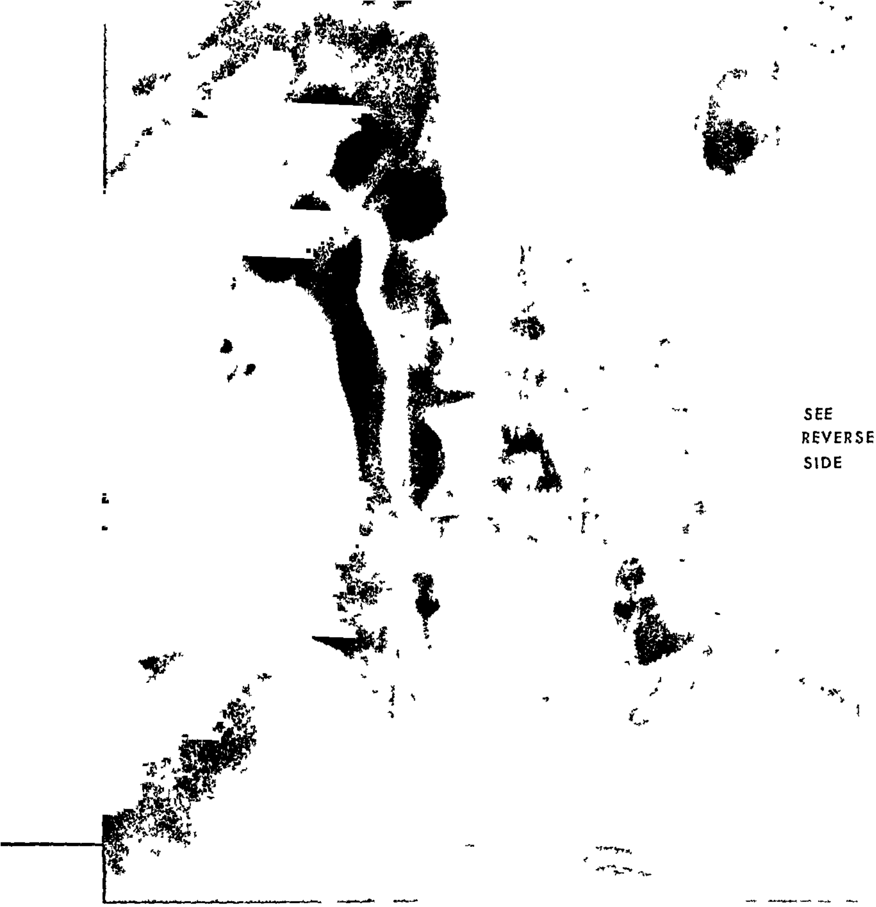
another new product



This is National's new, popular rechargeable battery 7100*. It has built-in recharger. It cuts out costly dry batteries of uncertain age. It puts a stop to lighting failure during cystoscopies or resections. Has a short circuit buzzer. Is ground-free, shock-proof, non-spillable. Lasts for years. Maintenance cost is trifling. For 110v. 50-60 cycles A.C.

CYSTOSCOPE DIVISION
NATIONAL ELECTRIC INSTRUMENT CO., INC.
92-21 CORONA AVE., ELMHURST, N. Y.

*Patent applied for.



SEE
REVERSE
SIDE

Intravenous urogram made with MIOKON Sodium 50%. Exposure twenty minutes after injection. Note double renal collecting system on the right with apparent joining of distal ureters

CLINICAL INVESTIGATIONS[1]

QUALITY OF PYELOGRAMS OBSERVED IN USING MIOKON SODIUM 50%

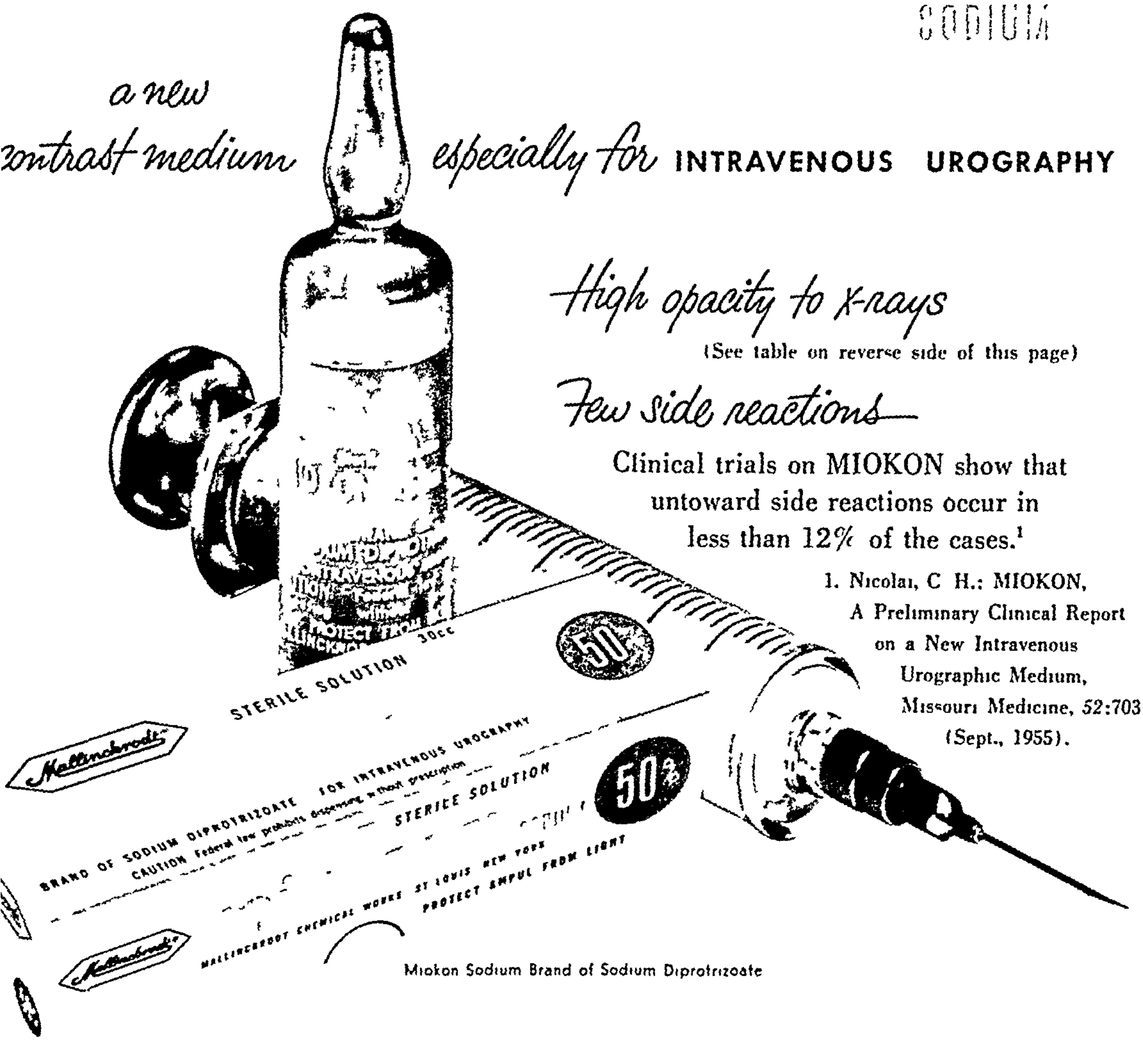
	PILOT STUDY	COOPERATIVE STUDY	TOTAL CLINICAL STUDY
TOTAL PATIENTS	1138	854	1992
GRADING OF PYELOGRAMS			
EXCELLENT	36.0%	26.4%	31.9%
GOOD	43.2%	59.7%	50.3%
FAIR	17.3%	9.2%	13.8%
PERCENTAGE DIAGNOSTIC FILMS	96.5%	95.3%	96.0%
POOR	3.5%	4.7%	4.0%

---

[1] a) Nicola C. H. MIOKON A Preliminary Clinical Report on a New Intravenous Urographic Medium Missouri Medicine 52 703 (Sept 1955)
b) Nicolai C. H. (Private Report dated July 19 1955 on 1138 cases)
c) Nicola C. H. MIOKON a New Intravenous Urographic Medium (To be published J. Urol.)

SODIUM

a new contrast medium especially for INTRAVENOUS UROGRAPHY


30cc
STERILE SOLUTION
Mallinckrodt
50
50%
BRAND OF SODIUM DIPROTRIZOATE FOR INTRAVENOUS UROGRAPHY
CAUTION Federal law prohibits dispensing without prescription
STERILE SOLUTION
MALLINCKRODT CHEMICAL WORKS ST LOUIS NEW YORK
PROTECT AMPUL FROM LIGHT
Mallinckrodt

High opacity to x-rays

(See table on reverse side of this page)

Few side reactions

Clinical trials on MIOKON show that untoward side reactions occur in less than 12% of the cases.[1]

[1] Nicolai, C H.: MIOKON, A Preliminary Clinical Report on a New Intravenous Urographic Medium, Missouri Medicine, 52:703 (Sept., 1955).

Miokon Sodium Brand of Sodium Diprotrizoate

MIOKON is produced by

Mallinckrodt makers of **UROKON®**

Urokon Sodium
Brand of Sodium Acetrizoate

UROKON SODIUM Sterile Solution is available in three different concentrations **UROKON 30%, UROKON 50%** (Standard) and **UROKON 70%** (Concentrated)

The specific techniques for which one or more concentrations of UROKON are widely accepted include **INTRAVENOUS UROGRAPHY, RETROGRADE PYELOGRAPHY, CHOLANGIOGRAPHY, ANGIOCARDIOGRAPHY, TRANSLUMBAR ARTERIOGRAPHY** and **NEPHROGRAPHY.**

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CHICAGO • CINCINNATI • CLEVELAND • DETROIT • LOS ANGELES • PHILADELPHIA • SAN FRANCISCO
IN CANADA **MALLINCKRODT CHEMICAL WORKS LIMITED** • 378 ST PAUL STREET W., MONTREAL

*Trademark

New urethral suppositories relieve pain and fight infection

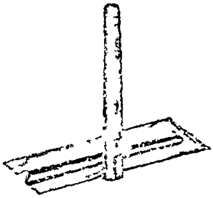
*For the patient, "The treatment is shorter and more comfortable than with the conventional method..."**

- suppository melts and releases anesthetic agent to relieve pain and burning *rapidly*
- kills most bacteria common to urinary tract
- easy for patient to insert at home
- *safe*—irritation rare in over 340 reported cases*
- *proved*—"The suppository method of medication has proved its worth."*. . . in bacterial (granular) urethritis, for prophylaxis and pain-relief before and after instrumentation.

to prevent cross-infection...

FURACIN® vaginal Suppositories are used with Furacin Urethral Suppositories to prevent cross-infection from the vagina Hermetically sealed in yellow foil Box of 12.

*Youngblood, V. H . J Urol 70 926, 1953



FURACIN®
BRAND OF NITROFURAZONE
urethral
SUPPOSITORIES

Each Furacin Urethral Suppository contains 0.2% Furacin (brand of nitrofurazone) and 2% diperodon HCl in a water-miscible base Hermetically sealed in silver foil Box of 12.

EATON LABORATORIES, Norwich, N Y. **NITROFURANS** a new class of antimicrobials neither antibiotics nor sulfas

instant, deep anesthesia of accessible mucous membranes

XYLOCAINE® JELLY ASTRA
(Brand of lidocaine*)

a new form of the widely accepted injectable Xylocaine Hydrochloride

- Provides more effective anesthesia of longer duration than any comparable preparation used in the genito-urinary tract, ear, nose and throat.
- Establishes immediate, intimate and prolonged contact with mucous membranes due to the low surface tension and high viscosity of its water-miscible base.
- Effectively lubricates for easier instrumentation.
- Nonstaining . . . easily removed with water . . . nonsensitizing and nonirritating.

Xylocaine Jelly contains 2% Xylocaine Hydrochloride in a sterile aqueous jelly adjusted to suitable viscous consistency with carboxymethylcellulose.

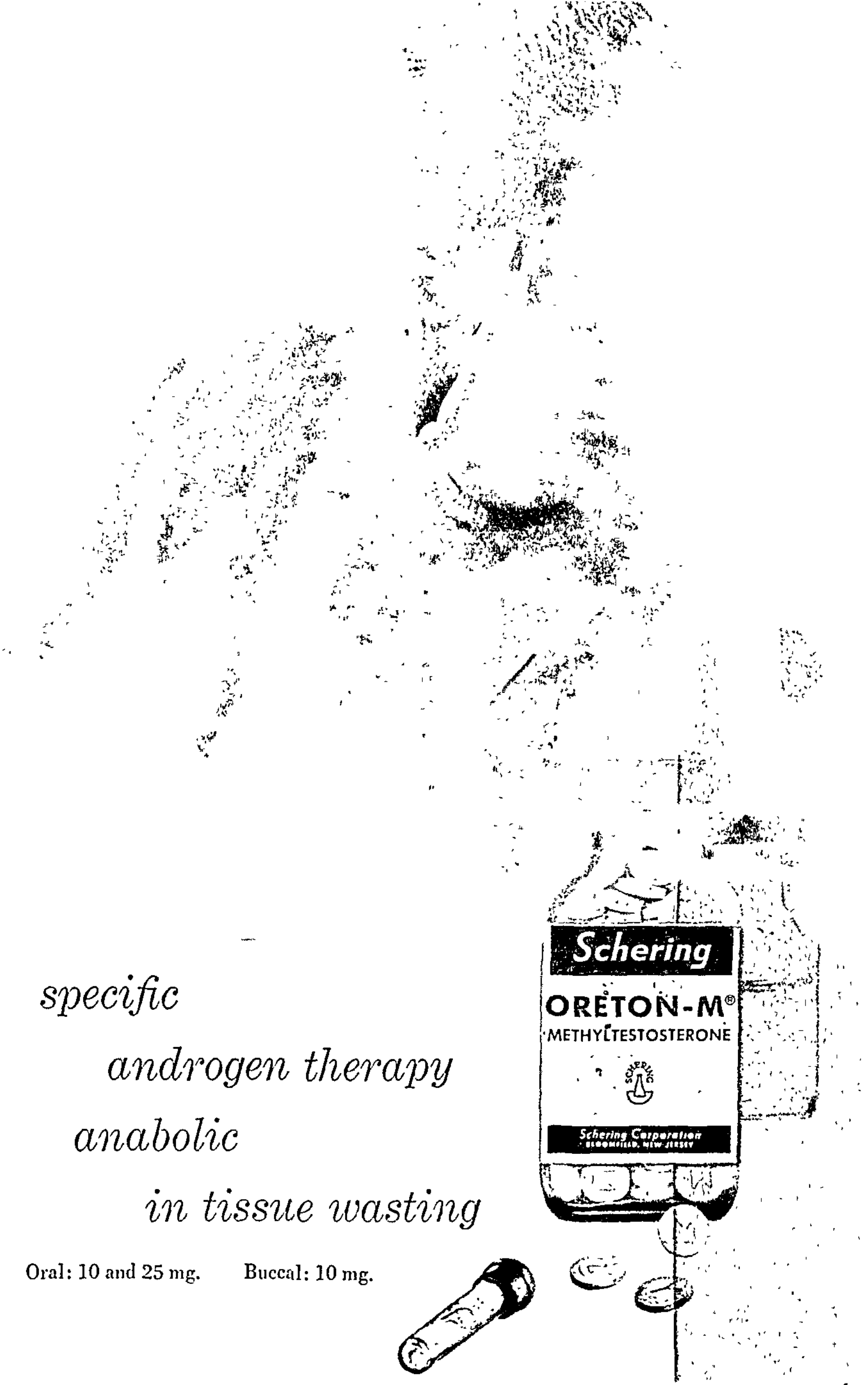
Supplied in collapsible tubes which deliver at least 30 cc.

A detachable applicator cone and a key for expressing contents are included in each package.

*U.S. Patent No. 2,441,498

Xylocaine Jelly is now made available at the request of many physicians, surgeons, and anesthesiologists who routinely use Xylocaine Solution.

ASTRA Pharmaceutical Products, Inc., Worcester 6, Mass., U.S.A.



specific

androgen therapy

anabolic

in tissue wasting

Oral: 10 and 25 mg. Buccal: 10 mg.

Perandren® phenylacetate
(testosterone phenylacetate CIBA)

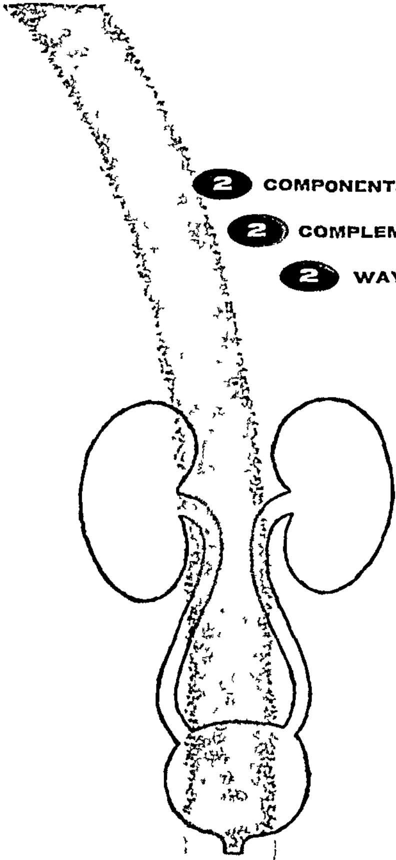
Clinically pre-eminent for potency and duration of androgenic/anabolic activity.

Usual schedule: One injection a month.

Usual response: Smooth improvement, due to potent, well-sustained androgenic and/or anabolic action.

Multiple-dose Vials, 10 ml., each ml. containing 50 mg. Perandren phenylacetate (with 1% procaine hydrochloride). 2/2224M

CIBA
SUMMIT, N.J.



2 COMPONENTS

2 COMPLEMENTARY ACTIONS

2 WAY CONTROL

—in urinary tract infections—

NOW . . . both *pain* and *infection* are brought under quick, safe control *at their source* by the speedy, dual action of the component drugs in—

*

RELIEVES LOCAL PAIN BY LOCAL ACTION
Phenylazo diamino pyridine HCl—enjoys a long clinical history as a local (not unwanted systemic) analgesic to the urogenital mucosa Relief from burning pain frequency—in minutes in 90 per cent of cases

REMOVES LOCAL INFECTION BY LOCAL ACTION
Sulfacetamide—sulfonamide of choice in urinary tract infections—unusually high solubility in acid urine so prevalent in pathological infections—hence (1) effective in 93 98 per cent of cases involving mixed organisms and (2) safe—no kidney damage no renal concretions no anuria

INDICATIONS
cystitis pyelitis urethritis (nonspecific) prostatitis pain and infection associated with kidney stones urinary prophylaxis during pregnancy and gynecologic surgery

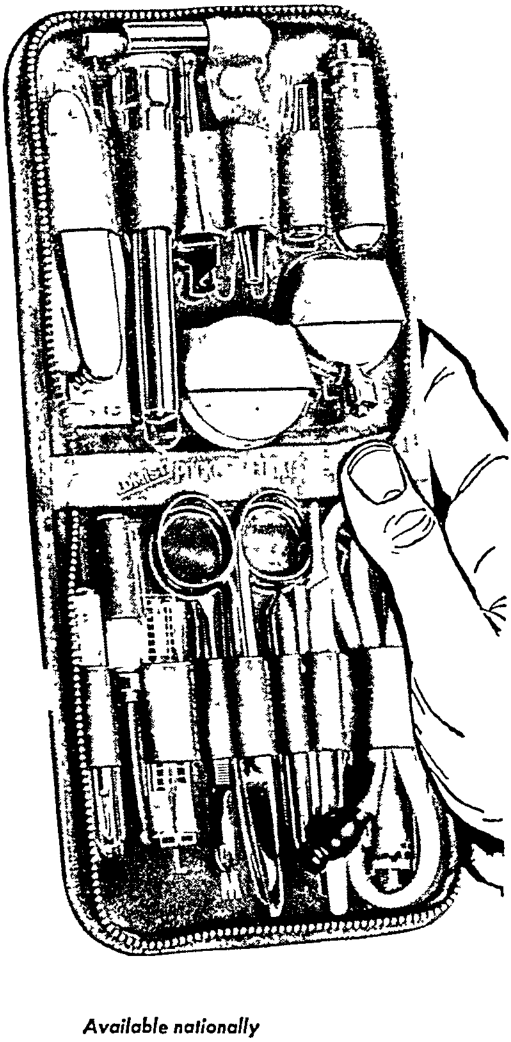
SUPPLIED
SULFID TABLETS each coated tablet contains Phenylazo diamino pyridine HCl 50 mg, Sulfacetamide 250 mg Bottles of 100
SULFID SUSPENSION (Geriatric–Pediatric)—each teaspoonful (5 cc) contains one half the Sulfid tablet dosage

COLUMBUS PHARMACAL COMPANY — Columbus 16, Ohio

Literature & bibliography on request.

*A Columbus Original Introduced July 1954

new compact **pocket medikit** of "essentials" for emergencies—



On vacations, motor trips, trains, planes, fishing and hunting trips, theatres, social events, etc.

—or for use in routine practice by those who do not usually carry a "black bag"

The Perfect Gift for a Colleague—or for yourself! Contains essential diagnostic instruments, therapeutic equipment and medications—in a compact leather case ***small enough to be carried in a pocket, purse or glove compartment.*** Send check or money order for $32.50.

Only 5 in. by 4½ in. by ¾ in.
13½ oz. complete!

Contents of Medikit—

Steel knife • Screw driver and file • Band-aids (May be replaced by plastic ruler with magnifying lens.) • Syringe and needle in sterile metal case with rubber cap • Reflex hammer with magnetized pin • 3 vials of medication for injection • Flashlight • Measuring tape (May be replaced by container for additional medications) • Stethoscope diaphragm • Suture material with swedged needle • Disposable cartridge of penicillin with sterile needle • Glass vials for medication • Tissue forceps • Scissors • Ballpoint pen and skin marker • Bard-Parker surgical knife handle and blade • Stethoscope tubing and attachments. May be used as a tourniquet • Thermometer in metal case.

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Available nationally only from

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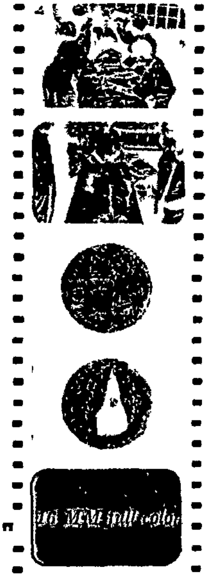

Announcing

a new medical motion picture

"The Value of Succinylcholine Chloride in Electroconvulsive Therapy and Laryngospasm"

demonstrating the effect of Quelicin during electroconvulsive therapy

from a sequence of unusual endoscopic shots showing the control of laryngospasm by Quelicin

in two versions: with sound, 12 minutes; silent, with subtitles, 25 minutes

602103

by
George J. Thomas, M.D.
Raymond L. Rau, M.D.
Robert J. Hudson, M.D.
of
St. Francis General Hospital
and Rehabilitation Institute of
University of Pittsburgh School of Medicine

with endoscopic scenes through the courtesy of, and based on the original work presented by:
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J. C. McClowery, M.D.
Veterans Administration Hospital
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University of Pittsburgh School of Medicine

Shows electroconvulsive therapy with and without the use of amnesic and muscle relaxant agents. Use of Pentothal Sodium (thiopental sodium, Abbott) to accomplish light anesthesia and amnesia of the event, as well as the use of Quelicin Chloride (succinylcholine chloride, Abbott) to reduce the convulsive contracture of skeletal muscles.

Abbott

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CHICAGO, ILLINOIS.

COMPARISON OF MAJOR HORMONAL EFFECTS OF ANDROGEN AND ESTROGEN ALONE AND IN COMBINATION

Effects	Androgen	Estrogen	Androgen plus Estrogen (Deladumone)
Metabolic Functions			
Protein tissue anabolism	+ + +	+	+ + + +
Bone tissue anabolism	+	+ + +	+ + + +
Psychic and nervous system equilibrium	+ +	+ +	+ + + +
Hormone Homeostasis			
Production of gonadotropin FSH	–	– – –	– – – –
LH	– – –	–	– – – –
Lut.H.	– –	– –	– – – –
Genital Organs and Accessory Sexual Structures			
Maleness	+ +	– –	O
Femaleness	– –	+ +	O

+ stimulated, – inhibited, O neither stimulated nor inhibited.

DELADUMONE

a new metabolic hormone preparation for enhanced therapeutic potential, greater safety and simplicity

Deladumone is Squibb testosterone enanthate and Squibb estradiol valerate combined in the most effective therapeutic proportion (approximately 20:1, by weight). With a single intramuscular injection—every 2 to 4 weeks[1]—Deladumone provides a balanced and integrated total metabolic effect. Deladumone assures:

an increased potential for...
- protein and osseous tissue anabolism
- correction of menopausal symptoms and hormone imbalance in the climacteric

a diminished potential for...
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Deladumone is indicated in: The menopausal syndrome; Osteoporosis in males and females.

Deladumone is supplied in vials of 1 and 5 ml., each ml. containing 90 mg. testosterone enanthate and 4 mg. estradiol valerate.

1. Skeels, R. F., and Shelton, E. K.: Clinical Research Proceedings 3:125 (April) 1955.

ALSO AVAILABLE **Delestrogen** (Squibb Estradiol Valerate) for timed action that ideally matches the estrogenic phase of the normal menstrual cycle (injectable). Vials of 1 and 5 ml., each ml. containing 10 mg. estradiol valerate. **Delatestryl** (Squibb Testosterone Enanthate), depot preparation for prolonged anabolic and androgenic effects (injectable). Vials of 1 and 5 ml., each ml. containing 200 mg. testosterone enanthate.

'DELESTROGEN', 'DELATESTRYL'® AND 'DELADUMONE' ARE SQUIBB TRADEMARKS

SQUIBB a name you can trust

**In 30 minutes–
antibacterial
action begins**

**In 24 hours–
turbid urine
usually clear**

*"...it appears that Furadantin is one of the most effective single agents available at this time."**

Furadantin®

BRAND OF NITROFURANTOIN

IN
URINARY
TRACT
INFECTIONS

- specific affinity for the urinary tract produces high antibacterial concentrations in urine in minutes—continuing for hours
- hundreds of thousands of patients treated safely and effectively
- rapidly effective against a wide range of gram-positive and gram-negative bacteria, including many strains of Proteus and Pseudomonas species and organisms resistant to other agents
- excellent tolerance—nontoxic to kidneys, liver and blood-forming organs
- no cases of monilial superinfection ever reported

SUPPLIED: Tablets, 50 and 100 mg. in bottles of 25 and 100.
Oral Suspension, 5 mg. per cc. bottle of 118 cc.

*Breakey, R. S.; Holt, S. H., and Siegel, D.: J. Michigan M. Soc. *54*:805, 1955

EATON LABORATORIES, Norwich, N.Y. **NITROFURANS** a new class of antimicrobials neither antibiotics nor sulfas

in urinary infections
TO MEET THE CHALLENGE OF CHRONICITY IN CYSTITIS • PROSTATITIS
URINARY CALCULI • UROLOGIC INFECTIONS OF PREGNANCY

℞ Mandelamine®
(Brand of methenamine mandelate)
Hafgrams®
0.5 Gm. (7½ gr.)

FOR EFFECTIVE LONG-TERM MANAGEMENT OF CHRONIC URINARY TRACT INFECTIONS

Mandelamine is effective, safe and specific in prophylaxis and treatment, even when used for prolonged periods. It sustains the patient in comfort by acting against both gram-positive and gram-negative organisms.

Supplied: Mandelamine Hafgrams—0.5 Gm. (7½ gr.) each, enteric-coated tablets, the new convenient dosage form for greater patient convenience, better patient cooperation.

Mandelamine 0.25 Gm. (3¾ gr.) each, enteric-coated tablets, for patients who require smaller doses, or prefer taking the smaller tablets.

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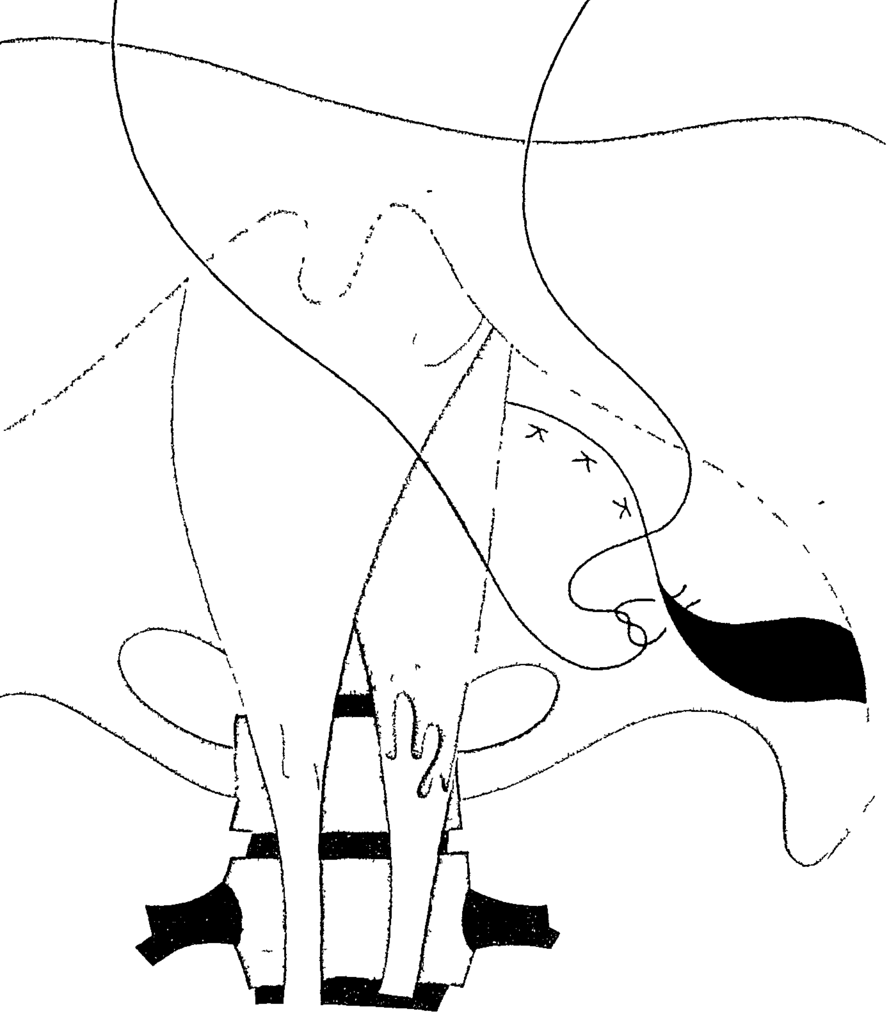

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silk or cotton
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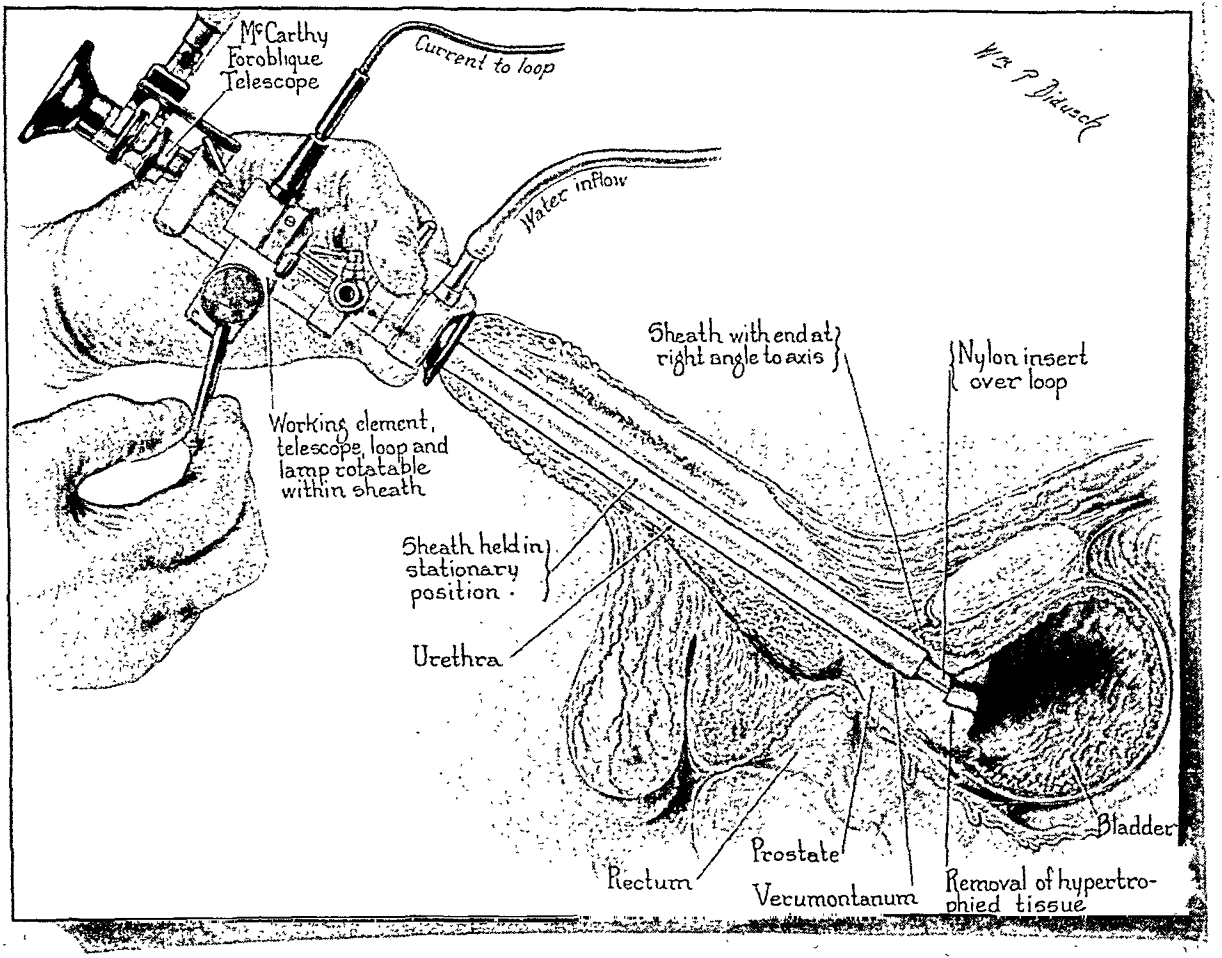
McCarthy Foroblique Telescope
Current to loop
W. P. Didusch
Water inflow
Sheath with end at right angle to axis
Nylon insert over loop
Working element, telescope, loop and lamp rotatable within sheath
Sheath held in stationary position
Urethra
Bladder
Prostate
Rectum
Verumontanum
Removal of hypertrophied tissue

Illustration depicts use of the McCarthy-Ritter Endourethral Resectoscope in the removal of hypertrophied prostatic tissue.

- Permits visualization of the entire lumen of the urethra without rotating the sheath.
- Permits visualization of pendulous urethra for study or surgery.
- The sheath has no fenestra, the end being rounded and cut off at right angles to the main axis of sheath.
- The working element fits into cone of sheath in such a manner that it may be rotated through a full 360° without moving the sheath. This reduces excessive manipulation of the sheath and the possibility of stricture of the urethra.
- A nylon insert covers the prongs of the loop, acts as a fenestra when at its furthest point from the end of the sheath and prevents tissue from falling between the prongs of the loop.
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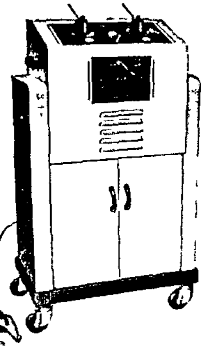
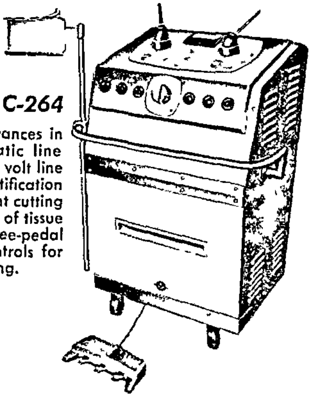
ESTABLISHED IN 1900
ACMI
BY REINHOLD WAPPLER

FREDERICK J. WALLACE, *President*
American Cystoscope Makers, Inc.
1241 LAFAYETTE AVENUE NEW YORK 59, N. Y.



A.C.M.I. Electrosurgical Unit C-264

Incorporates the most recent advances in electronic engineering; automatic line voltage regulator to stabilize 115 volt line current . . . full wave oscillator rectification . . . extra power output for efficient cutting or coagulation without destruction of tissue or damage to instruments . . . three-pedal footswitch and optional dial controls for individual precision at each setting.

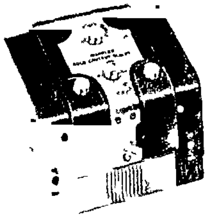


Wappler Surgical Unit C-263 RC

Special electronic circuits for delicate telescopic instruments . . . abundant power . . . elective dial settings . . . cutting and coagulation on completely independent circuits . . . economical and adaptable.

A.C.M.I. Electrosurgical Equipment provides the highest standard of excellence for surgeons who can accept nothing less

A.C.M.I. ELECTROSURGICAL EQUIPMEN



Wappler Cold Cautery Scalpel C-450

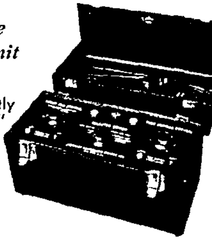
Small, compact, light weight (16 lbs.) for office or hospital use . . . high frequency cutting and coagulation with special 'cold' electrode to reduce heat radiation . . . simple control panel and shock-proof footswitch . . . 6-foot conducting cords housed in case with rewind mechanism under push-button control.

Surgeons have long esteemed A.C.M.I. electrosurgical equipment as the finest consummation of engineering design and clinical serviceability available, for use in all branches of general surgery. Their exquisite craftsmanship provides the perfect instrumental medium for peerless surgical technique. A variety of models is provided, to serve the individual physician's requirements.

Visit your dealer to inspect these modern electrosurgical units and their accessories, or write for complete information.

A.C.M.I. Portable Electrosurgical Unit C-350

Compact and conveniently portable . . . 18½" x 14¼" x 8⅜" . . . only 33 lbs. complete, with 8 electrodes and other accessories . . . independent separate circuits for cutting and coagulation of any tissue.



Units C-263 RC and C-450 are available in 3 models for 110-120 or 220 240 volt, 50 60 cycle A C., and for 110 volt, 25 cycle A C.; Unit C-350 for 110-120 and 220-240 volt, 50 60 cycle A C.; Unit C-264 is designed to operate at 110-120 volt, 50-60 cycle A C. The automatic voltage regulator permits satisfactory operation between 90 and 135 volts.

ESTABLISHED IN 1900 · BY REINHOLD WAPPLER

FREDERICK J. WALLACE, *President*

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a new, powerful bactericide . . .

Available in pure crystal form in packages of 3.8 Gm. sufficient to make 1 gallon of 1:1000 solution or tincture; also:

Tincture ....1:500 } 8 oz. and 1 gal. bottles
Tincture 1:1000
Aqueous Solution..1:1000

Urolocide—a new non-toxic quaternary ammonium compound of unprecedented bactericidal efficiency—marks an important step forward towards the realization of the surgeon's dream of optimum antisepsis . . . Urolocide is an all-purpose disinfectant containing no phenolic, mercuric or other corrosive ingredient, yet it is rapidly bactericidal and fungicidal—in highest dilutions—against a wide range of commonly occurring pathogens (both gram-positive and gram-negative). Urolocide possesses extraordinary detergent and penetrating properties and is non-irritating to human tissues. It is odorless, colorless, non-staining and water-soluble . . . Urolocide's range of usefulness in major and minor surgery, obstetrics, gynecology, genito-urinary infections, dermatology and proctology is almost universal. Also, for the cold disinfection of instruments and for general hospital use, Urolocide is an equally efficient disinfectant . . . A complete descriptive brochure on the chemistry, pharmacology and clinical uses and applications of Urolocide will be sent on request.

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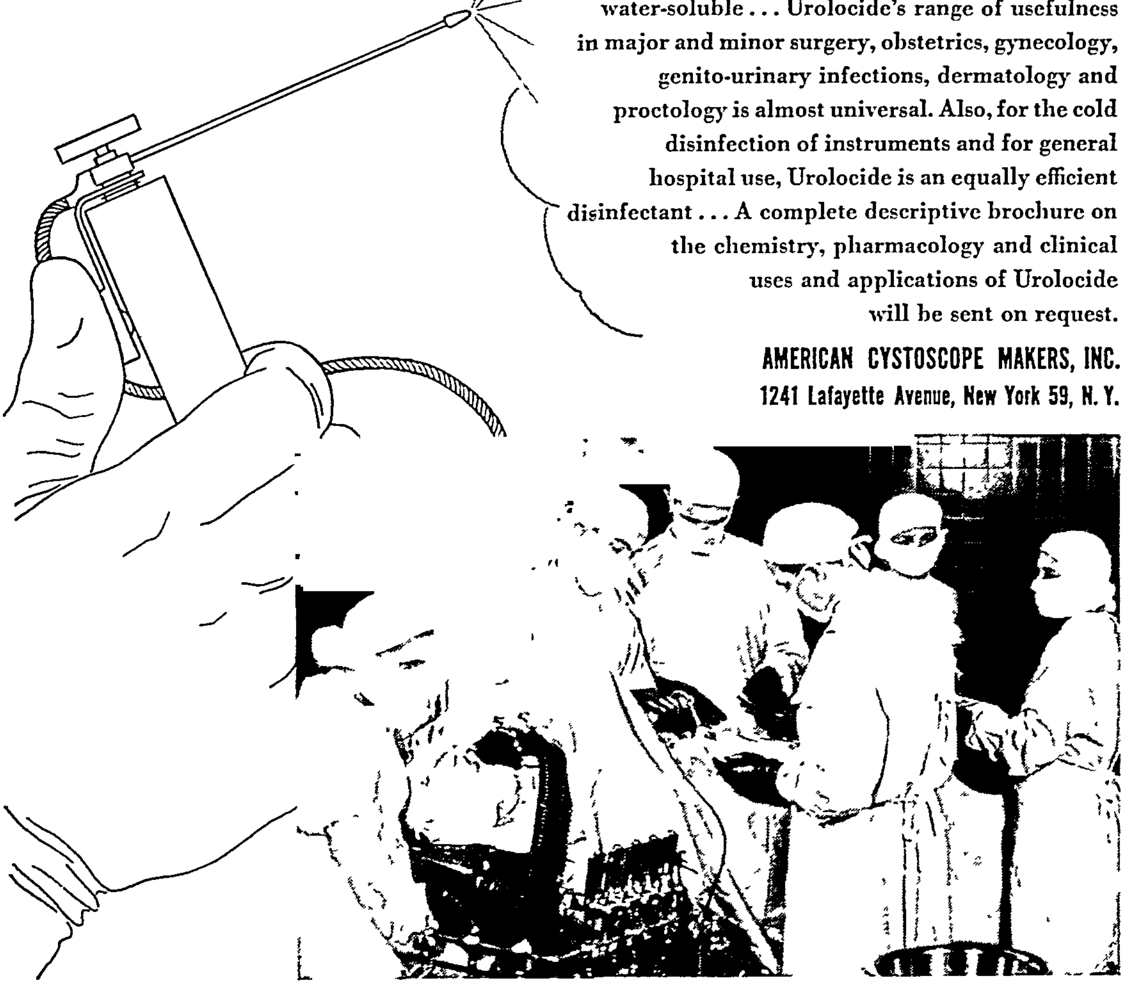

The Journal of Urology
Vol 75, No 2, February 1956
Printed in U.S.A.

CONGENITAL URINARY TRACT OBSTRUCTIONS IN CHILDREN

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The purpose of this presentation is to report our experiences in the management of congenital obstructive uropathies in children and their associated problems with particular emphasis on extended followup observations. The chief difficulties in these cases reside in the fact that many of these children are in a precarious state of health. Thus, initial treatment and successive measures are intimately related in the sense of determining a course of reparative operative procedures. In the course of events of simple, uncomplicated congenital obstructions of the kidney, ureter, or bladder neck, prostatic valves, or stricture of the urethra, the problem of management is basically identical with management of similar lesions in the adult. This type of case is readily managed according to conventional methods. It is obvious that one must have considerable familiarity of the methodology of study, evaluation of the pathologic physiology, renal integrity, neuromuscular dysfunction of the parts involved with either primary or secondary complications. In case of a congenital hydronephrosis without any secondary complications, the modus operandi is well known. On the other hand, if the hydronephrosis is bilateral and there is marked variance in renal capacity, the question of salvage of both kidneys is the pressing problem. In such instances it is well to know that it is necessary to operate on the poorer kidney first and then within a short period of time repair of the better kidney is done.

According to Hinman, renal repair occurs only if there is renal stimulation. If this does not occur there is no change in the renal dysfunction; in fact, it may and usually does progress to a functionless state. Unless the poorer kidney is forced to carry the load following operation on the better kidney, the concept of renal stimulation is not appreciated. Rich states, "There are two basic fundamentals of all surgery in hydronephrosis: 1) nephrectomy of the kidney without life sustaining function if the opposite kidney demonstrates normal function; and 2) repair of the poorer kidney first, followed in a short time by the repair of the less disturbed kidney, if there is bilateral obstruction." If one follows these basic facts the problem of management may be appreciated more readily.

The multiplicity of operations is one point which must be mentioned. The initial treatment may consist of various operative procedures to obtain satisfactory drainage of urine. Definite operations to correct the obstruction cannot be carried out until satisfactory function of the kidney or kidneys is obtained. In many cases definite procedures can never be done because of this fact, then the child is maintained permanently on some form of tube drainage. It is necessary to keep these children under more or less continuous observation in order to maintain proper drainage. Change of tubes is one of the real problems confronting such children because temporary stoppage and or blockage will frequently

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Read at annual meeting, American Urological Association, Los Angeles, Calif. May 16–19, 1955.

cause superinfection and result in progress of renal dysfunction. Obviously this same basic principle is necessarily important in the repair stage, since many cases have either been preceded by a nephrostomy or pyelostomy and renal drainage must be obtained by such procedures following the repair of the obstruction. Multiplicity of operative procedures, therefore, is no longer the exception but indeed rather common. The same principle and concept have been practiced by the urologists for many years in correction of congenital abnormalities of the external genitalia. Despite many reports to the contrary, fistulas, strictures and persistence of chordee are responsible for repetition of operative procedures in the correction of hypospadias. These children need constant care. Maintenance of drainage is so absolutely necessary that many of the poor results can readily be attributed to improper attention by the house staff, both physicians and nurses, and poor home care. It is interesting to note that frequently we find that the care given to these children in the poorer homes is considerably better than in the higher income group. There are several reasons for this, namely, the parents have a tendency to bring their child promptly to the hospital if the tubes do not drain properly; others may call their own physician who may try to manage the problem and hospitalization is delayed. The group of children in the lower economic echelon are also more prone to listen to reason and will follow the physician's instructions exactly. Generally it is quite necessary to instruct the parents of these children very carefully.

The incidence of congenital obstructions in the urinary tract varies considerably in the different clinics. From the standpoint of a large general hospital it has been noted that there is gradual annual increase in the number of children who are studied urologically. We have indeed come a long way in this regard and much credit belongs to Campbell and all others who have stimulated interest in pediatric urology. This does not necessarily entail the development of another sub-specialty. It seems to us that if one is trained in an understanding of basic urologic principles associated with obstructions he should be able to cope with these problems in children as well as similar conditions in the adult. For this reason it is well to emphasize the necessity for the urologist to become skilled in the use of the smaller cystoscopic instruments. Technical difficulties must be recognized. One must be familiar with anatomical variants and pathological changes. Herein lies the importance of education of our colleagues if we are to maintain and increase our prominence in this particular field of urology. No one is better trained to manage these lesions than the urologist. However, the training and experience must be such that the urologist has the confidence of the parents, the family physician and, in many instances, the pediatrician. The tendency for the pediatric surgeon to undertake these problems must be appreciated, primarily because they have developed operative techniques and postoperative care peculiar to children only.

During the 5-year period from 1950 to 1954 there were 369 pediatric urologic cases at the Jefferson Hospital. On these patients a total of 466 procedures were carried out in the operating room. Of these 132 were diagnostic cystoscopies, 152 were cystoscopic operative cases and 182 were surgical operative cases (table 1).

TABLE 1 *Pediatric urology, Jefferson Hospital*
5 Yrs 1950-54
Total Cases—369
Total Procedures—466

Diag Cysto	Cysto Operative	Surg Operative
132	152	182

TABLE 2 *Congenital obstruction in children*

Kidney & Pelvis

- Ureteropelvic
  - vessel
  - stricture
  - fibrous band
- Reduplication
- Horseshoe
- Ectopia
- Hypoplasia

Course of Ureter

- Vessel
- Fibrous band
- Double ureter
- Atonic (megaloureter)
- Retrocaval
- Ureteral valves

Ureterovesical

- Stricture
- Ureterocele
- Double ureter
- Incompetent valve with reflux

Bladder

- Neurogenic (megalobladder)
- Contracture
- Exstrophy
- Diverticulum

Ectopic Ureteral Orifices into

- Seminal vesicle
- Bladder
- Vagina
- Urethra
- Diverticulum
- Ejaculatory duct
- Vas deferens
- Rectum
- Uterus
- Fallopian tubes

Bladder Neck & Urethral

- Contracture vesical orifice
- Polyp prostatic urethra
- Hypertrophy verumontanum
- Posterior urethral valves
- Urethral stenosis
- Ext meatal stricture
- Aplasia of urethra
- Epithelial occlusion of urethra
- Diverticulum of urethra
- Hypospadias
- Epispadias

Obstructions of congenital nature include more than the classical "narrowing" or "stricture" at a point along the urinary passageway There are numerous other instances where the factors of reduplication, ectopia of position, course and termination, hypertrophy, aplasia and neurogenic disorder, to mention a few, are quite sufficient to cause obstruction and loss of renal function (table 2)

The problems encountered in the management of many congenital obstructions in children are frequently so discouraging that one hesitates to report cases which may not have been treated in conventional manner and this precludes wide acceptance of the methods used It is appreciated that the difficulties frequently appear insurmountable It is a vast field for new techniques and possibly im-

TABLE 3. *Surgical operations*

Upper Tract		*Lower Tract*	
Nephrectomy	11	Hypospadias repair, all stages	64
Intubated ureterotomy	9	Plastic repair of penis	17
Explor. laparotomy	5	Orchiopexy	11
Nephrostomy	3	Hydrocelectomy	10
Partial ureterectomy	2	Herniorrhaphy	7
Hemisection of kidney & ureter	1	Ureterosigmoid transplant	6
Bilat. reimplantation of ureters into bladder	1	Suprapubic cystotomy	4
Heminephrectomy	1	Epispadias repair	3
Nephropexy & ureterolysis	1	Miscellaneous (change tubes, remove sutures, biopsy, explor.)	24
Excision of renal cyst	1		
Pelviolithotomy	1		146
	36		

Total—182

provement of many of the older procedures which may have gained recognition by virtue of experience.

It is the intent of the authors to present representative cases of congenital obstructive lesions in children with particular emphasis on long-term management.

Table 3 is a more specific outline of the surgical operative cases reviewed. From these we have selected seven representative cases for discussion.

CASE REPORTS

Case 1. L. W., an 8-year-old white girl, was admitted to the Jefferson Hospital because of left abdominal pain of 4 years' duration. Two years previously, she had gross hematuria and she had been hospitalized elsewhere. On admission there was microscopic hematuria, 8–10 white blood cells per high powered field. The urine was uninfected. Blood urea 10.3 mg. Phenolsulfonphthalein output: 60 per cent in 30 minutes.

Figure 1, *A* and *B* show the excretory urogram and retrograde pyelogram. Ureteropelvic obstruction with pelviectasis was noted on the left side. On July 23, 1954 intubated ureterotomy was done; the ureter was splinted with a No. 10 red rubber tube placed 10 cm. down the ureter and the proximal end brought out through the inferior calyx adjacent to a nephrostomy tube. This splint tube remained in place 28 days. Several ostia were cut into the splint tube at the point where it passed through the renal pelvis. In this case a No. 20 Foley catheter with the tip cut off proximal to the balloon was used as the nephrostomy tube. Both these tubes therefore permitted excellent sites for irrigation of the tubes and interior of the collecting system with acid solution such as ⅛ per cent acetic acid during the postoperative intubation. We wish to emphasize the necessity for maintaining the system free of phosphatic deposits and that acid irrigations must be started several days postoperatively before the alkaline encrustations have the opportunity to form.

Figure 1, *C* and *D* show the antegrade pyelogram made at the time the splint

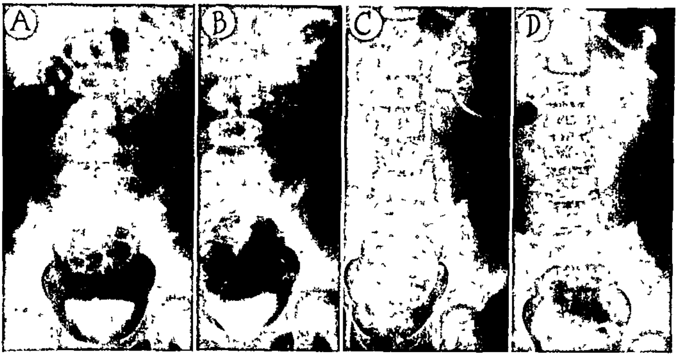

FIG. 1. Case 1. *A* and *B*, preliminary excretory urogram and retrograde pyelogram delineating ureteropelvic obstruction with pyelectasis on left, impaired function on right due to hypoplastic kidney. *C*, antegrade pyelogram made at time splint tube was removed. *D*, followup retrograde pyelogram (evacuation) 8 months later.

tube was removed and retrograde study done in April 1955. The child is completely asymptomatic, the urine is negative for red blood cells and bacteria. While the calyceal pattern is sharp, there still appears to be the same degree of pelvic retention.

Comment: The obvious difficulty in these cases is to properly evaluate the children by repeated studies. The original decision in this case was to remove the left kidney. For this reason another opinion was suggested. If one studies the excretory urogram carefully the right kidney is almost hypoplastic although symptomless. Removal of the left kidney would, under the circumstances, have been hazardous. The premise that the poorer kidney should be operated upon first was not seriously considered here because the child really had only one fairly good renal system. Differential studies of function may be difficult in children but they are indeed essential.

Case 2. S. M., a 6-year-old white boy, was admitted to the Jefferson Hospital on August 12, 1948 with a temperature of 104.4F, severe dysuria, and lower abdominal pain. Two years earlier the patient had been studied at another hospital. He had a nonfunctioning right kidney, a large diverticulum of the bladder, vesical neck obstruction due to median bar, and left hydronephrosis and hydroureter. The blood urea was 36.4 mg. and the phenolsulfonphthalein excretion 15 per cent in 1 hour. The urine was uninfected. Suprapubic cystotomy with resection of median bar, diverticulectomy, division and ligation of the right ureter at the bladder level and left ureteral meatotomy had been carried out prior to our seeing the patient.

Figure 2, *A*, *B* and *C* show the cystogram and excretory urogram on admission. Suprapubic cystostomy was re-established.

On November 18, 1948, a right nephrectomy was done. After 3 months of drainage the blood urea was 13.6 mg. and the phenolsulfonphthalein output

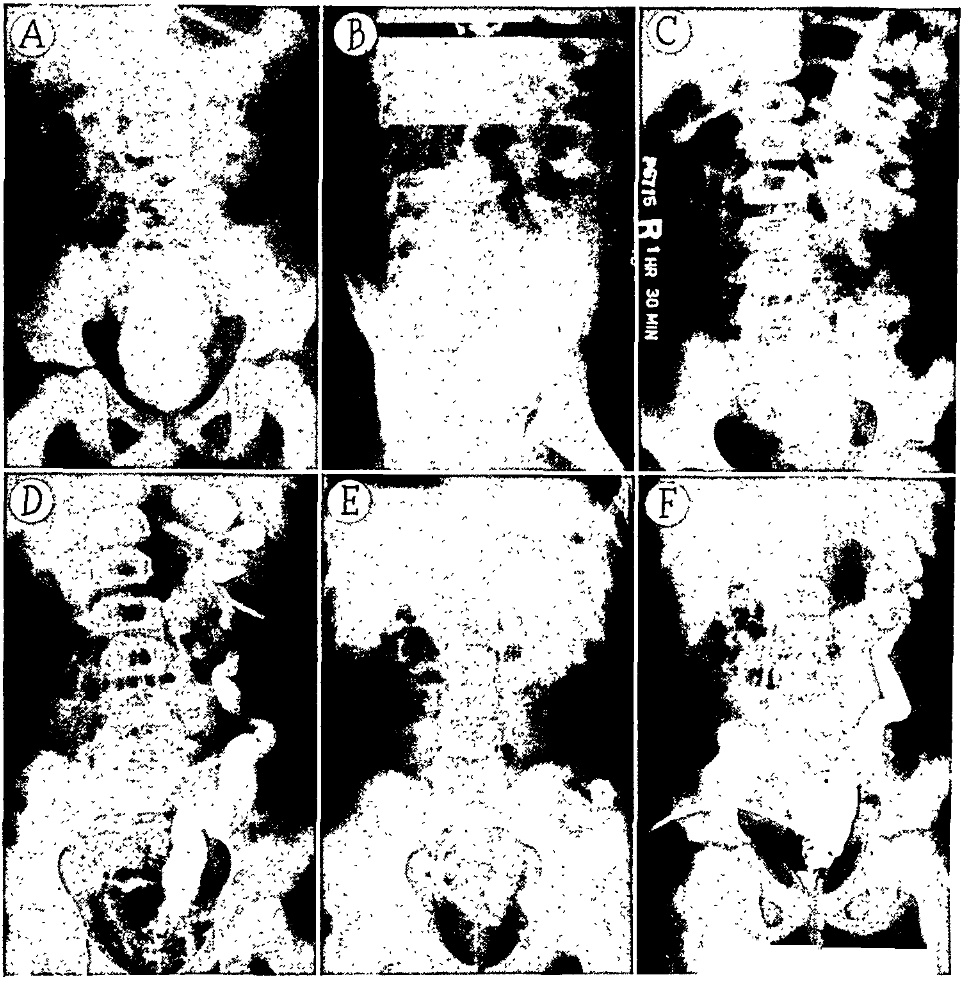

FIG. 2. Case 2. *A* and *B*, cystogram showing large diverticulum. *C*, excretory urogram showing massive hydronephrosis and tortuous, dilated ureter. *D*, antegrade pyelogram after 5 years of drainage. *E*, excretory urogram 7 years after initial therapy. *F*, cystogram showing vesicoureteral reflux.

45 per cent in 30 minutes. On February 2, 1949, diverticulectomy, left ureteral meatotomy and a wedge resection of the vesical neck were accomplished. The patient was discharged on suprapubic drainage.

Two years later the boy was readmitted because of an increase in the degree of hydronephrosis. Indigo carmine appeared in 5 minutes but the left ureteral orifice could not be catheterized. On March 16, 1951, left nephrostomy was established. On January 13, 1953, the left ureteral orifice was identified and meatotomy done. Three months later the left ureteral meatotomy was extended. The patient then ran a febrile course for 6 weeks. The urine was infected with Pseudomonas aeruginosa resistant to all the antibiotics. It was at this time that *we first used furadantin. The result was encouraging in that the infection was* brought under control and the child was sent home with both nephrostomy and suprapubic drainage.

Figure 2, *D* shows the antegrade gyelogram at that time. In January 1954, the nephrostomy tube became dislodged and there was an 8-day delay in the child's reporting to the hospital. Usual methods short of surgical exposure were unsuccessful in an attempt to replace the nephrostomy tube. Urography displayed what appeared to be an adequate ureterovesical junction and therefore the nephrostomy site was allowed to close. During the following year the urine remained uninfected, the blood urea unchanged at 27 mg., and the phenolsulfonphthalein output 15 per cent in 30 minutes.

Figure 2, *E* and *F* show the excretory urogram and cystogram done in April 1955. The incompetency of the ureterovesical mechanism is displayed by the reflux filling the entire upper tract.

Comment: Here is a boy aged 13 who has been a urologic cripple since birth. Extensive ureteral meatotomy was necessary before an adequate orifice could be obtained. Our efforts in this regard were apparently more than adequate as evidenced by the reflux now present. Failing renal function required not only continuous cystostomy drainage but nephrostomy drainage for 34 months. We were impressed with the excellent response to furadantin, despite the progressive renal insufficiency, at the time that the child appeared doomed with superimposed pyelonephritis. While it is doubtful that his renal function will ever permit further correction the child is well adjusted to his suprapubic tube and is attending school. He was recently seen for replacement of his tube which came out while he was playing soccer.

Case 3. N.T., a 4-year-old white girl, was first treated by the pediatric department for pneumonia and pyelitis in 1952. On February 2, 1953 she was admitted to the urologic service at the Jefferson Hospital with chills, fever, bilateral costovertebral pain and grossly infected urine. The initial excretory urogram was reported as normal by the x-ray department, but a review of the films revealed a filling defect in the bladder suggestive of ureterocele. This was confirmed on cystogram and ureteral reflux was noted on the left. Blood urea 10.3 mg.; phenolsulfonphthalein excretion 37 per cent in 30 minutes.

On March 3, 1953 the right ureterocele was resected transurethrally revealing a large ostium at the normal site of the right ureteral orifice. The left orifice was normal in position and appearance. Further excretory urography and right retrograde pyelography revealed reduplication of the right upper urinary tract; the upper portion and its ureter were markedly hydronephrotic. The ureter to the lower half was slightly dilated and the two appeared to join at the juxtavesical or intramural level.

Figure 3 shows the initial cystogram. The repeat excretory urogram and right retrograde pyelogram are shown in figure 4.

On April 10, 1953, right heminephrectomy and partial ureterectomy of the upper hydronephrotic kidney and its ureter were accomplished. There was a double kidney each with its own blood supply. The dilated ureter from the upper kidney joined with the ureter from the lower kidney 2.5 cm. from the bladder. When the dilated ureter was opened where it joined the good ureter we were unable to demonstrate an ostium. The remaining ureter was dilated antegrade to accept a No. 8 ureteral catheter and this was fixed indwelling.

In January 1954, the patient was found to have a B. proteus infection which responded to furadantin. Periodic urethral dilatation followed.

The patient was readmitted on February 8, 1955 because of a low grade fever and malaise. The blood urea was 13.6 mg. and the phenolsulfonphthalein output 35 per cent in 30 minutes. The urine culture grew Friedlander bacillus. Cystoscopy revealed a small, shallow diverticulum 0.5 cm. in diameter and depth just

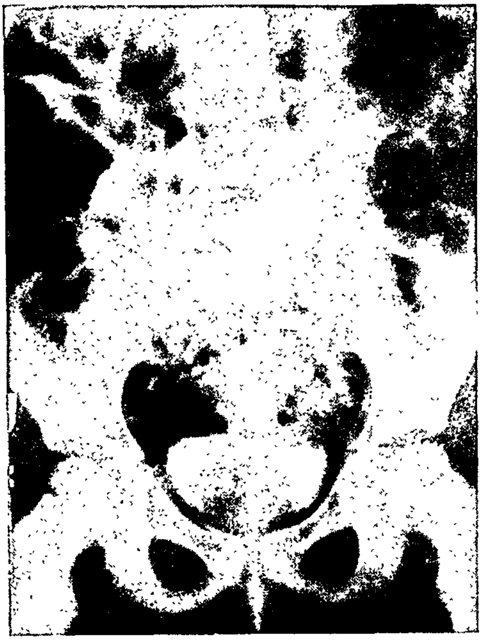

FIG. 3. Case 3. Initial cystogram showing large filling defect

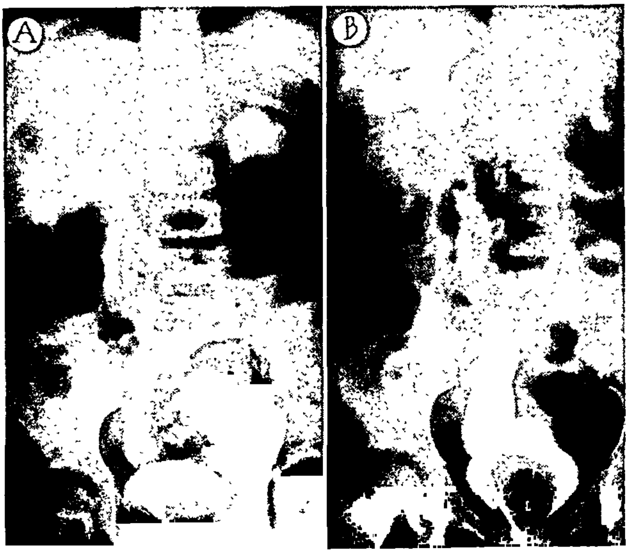

FIG. 4. Case 3. *A*, initial excretory urogram showing bilateral hydronephrosis and reduplication of right upper tract. *B*, retrograde pyelogram showing hydronephrotic superior half and its ureter.

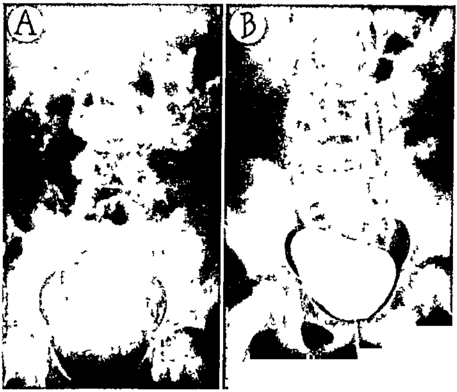

FIG. 5. Case 3 *A*, excretory urogram 2 years after operation. *B*, cystogram showing vesicoureteral reflux.

in front of the right ureteral orifice. The latter was slit-like but approximately one centimeter in length. The left ureteral orifice was ovoid and patent at all times. The vesical orifice displayed an elevation of the posterior lip which was fulgurated with the conical electrode and the urethra dilated to 26F.

Figure 5 shows the excretory urogram and cystogram at this time.

The patient is to be readmitted at the close of the present school term and the left ureter will be reimplanted into the bladder in an attempt to eliminate the reflux to the left upper tract.

Excretory urograms on the patient's mother and sister reveal congenital anomalies but they have been asymptomatic.

Comment: The entire problem with this child unfolded when an almost overlooked filling defect in the bladder was further investigated. Aside from the reduplication it will be necessary to deal with another congenital defect, that is, the incompetent ureterovesical mechanism of the opposite side.

Case 4. Twelve hours after his birth B. D. was operated on for hernia of the anterior abdominal wall. At the age of 3 months he began to have pain on voiding. At the age of 5 years he had what the parents described as a "block in the bladder" with hematuria and pain on voiding. The "block" was removed by suprapubic cystotomy but 5 months later, because of straining and frequency, the tube was replaced. The child, then 6 years old and with a suprapubic tube still in place, was admitted to the Jefferson Hospital on May 8, 1952. A 16F panendoscope was passed with difficulty. The vesical orifice was open. There were folds in the prostatic urethra and around the verumontanum which may have been valves. There was slight trabeculation of the bladder. The right ureteral orifice was normal in appearance, but located high on the right wall. The left orifice was "golf-hole" in shape. Careful inspection revealed two ureteral orifices; the upper was slit-like while the lower was rounded and remained open.

Both emptied into the previously mentioned "golf-hole" orifice. Blood urea 17.6 mg.; total phenolsulfonphthalein output 50 per cent in 30 minutes. The bladder capacity was 300 cc and urine was voided per urethram in a small but forceful stream. The residual urine removed through the suprapubic tube was 175 cc. X-rays showed reduplication of the upper urinary tract bilaterally. On the right, there was a marked hydronephrosis of both upper and lower pelves and both ureters. The left lower pelvis and ureter were markedly dilated while the left upper pelvis, calyces and ureter were very delicate, indicating that the obstruction was probably intrinsic in the ureters rather than being all due to urethral resistance.

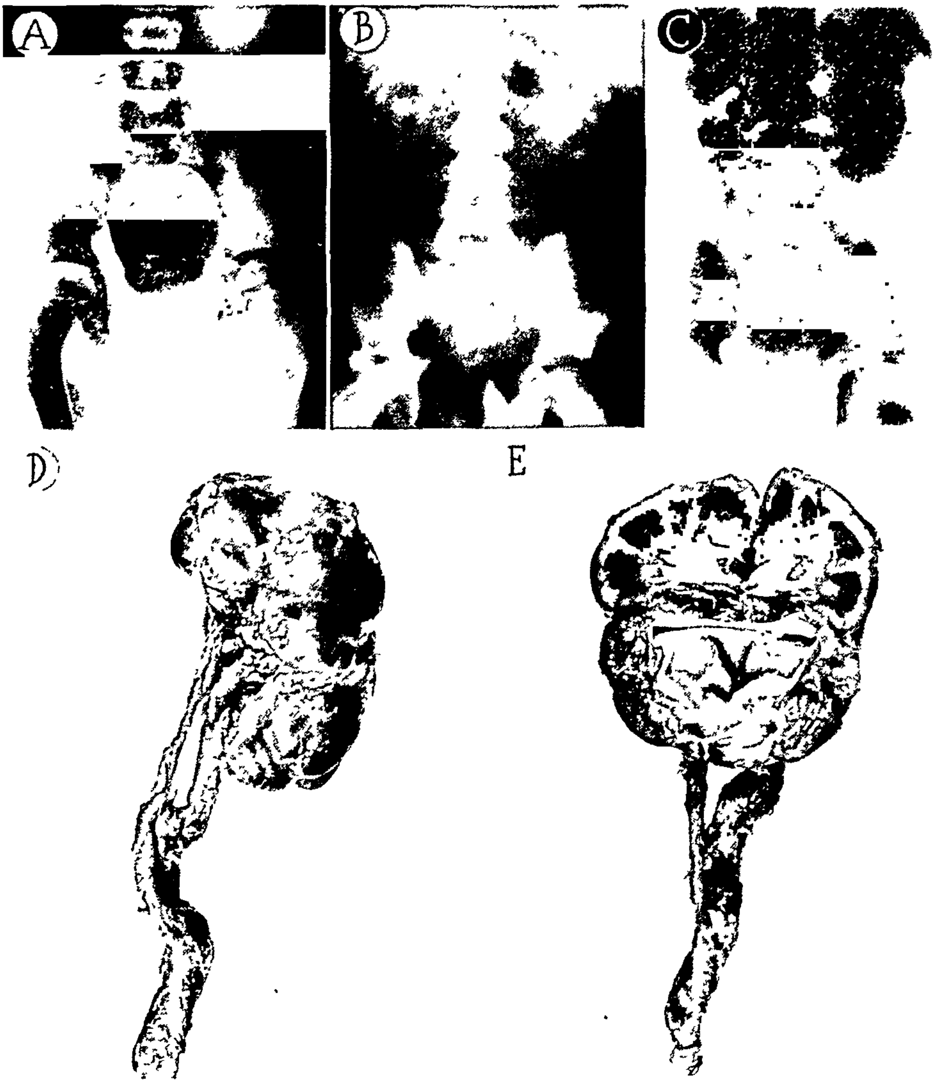

FIG. 6. Case 4. *A*, cystogram on admission showing reflux on left. *B* and *C*, excretory urograms on admission showing bilateral reduplication with hydronephrosis of both upper and lower systems on right, lower pelvis and ureter on left. *D* and *E*, left upper tract, gross specimen

Figure 6, *A*, *B* and *C* show the cystogram and intravenous urogram on admission.

On June 19, 1952 the right upper tracts were surgically exposed. At the level of the iliac artery dilated ureters were found and also a dense, fibrous sheath surrounding both ureters. The sheath was dissected and a stenotic portion exposed, 4 cm. from the bladder, where the lateral of the two ureters joined the medial, proceeding as a common ureter into the bladder. A constricting septum between the ureters at the junction was divided for a distance of two centimeters and each ureter intubated with a No. 8 red rubber catheter extending from their respective renal pelves into the bladder and out the cystotomy wound. The splint tubes remained in place for 1 month. Periodic urethral dilatation was continued and on March 18, 1953, the left upper tract was surgically exposed with the hope of doing a heminephroureterectomy to remove the lower hydronephrotic portion and its ureter. A single kidney with one pedicle and double collecting systems and ureters were found so that nephrectomy and complete removal of both ureters were carried out.

Figure 6, *D* and *E* show this gross specimen.

Two months later the suprapubic fistula was closed and the patient discharged. The child is now 8 years of age, and enjoying good health.

Figure 7 shows the excretory urogram made in April 1955.

Comment: This child had been ill since birth with multiple congenital anomalies. It again demonstrates the necessity for complete urologic investigation with considerable thought as to subsequent management. The period of preliminary and continued drainage during the course of surgical correction is emphasized to obtain good results.

Case 5. C.N., a 7-year-old adopted white boy, was admitted to an upstate Pennsylvania hospital in September 1953 because of a urinary tract infection. Prior to this he had enjoyed good health. A diagnosis of agenesis of the right kidney and vesical neck obstruction was made and the patient placed on supra-

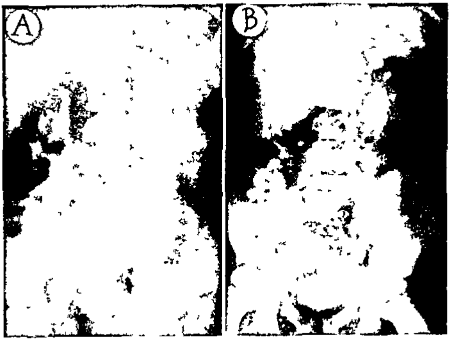

FIG. 7 Case 4 *A*, 10-minute and *B*, 60-minute films of excretory urogram made 1955, three years after operation.

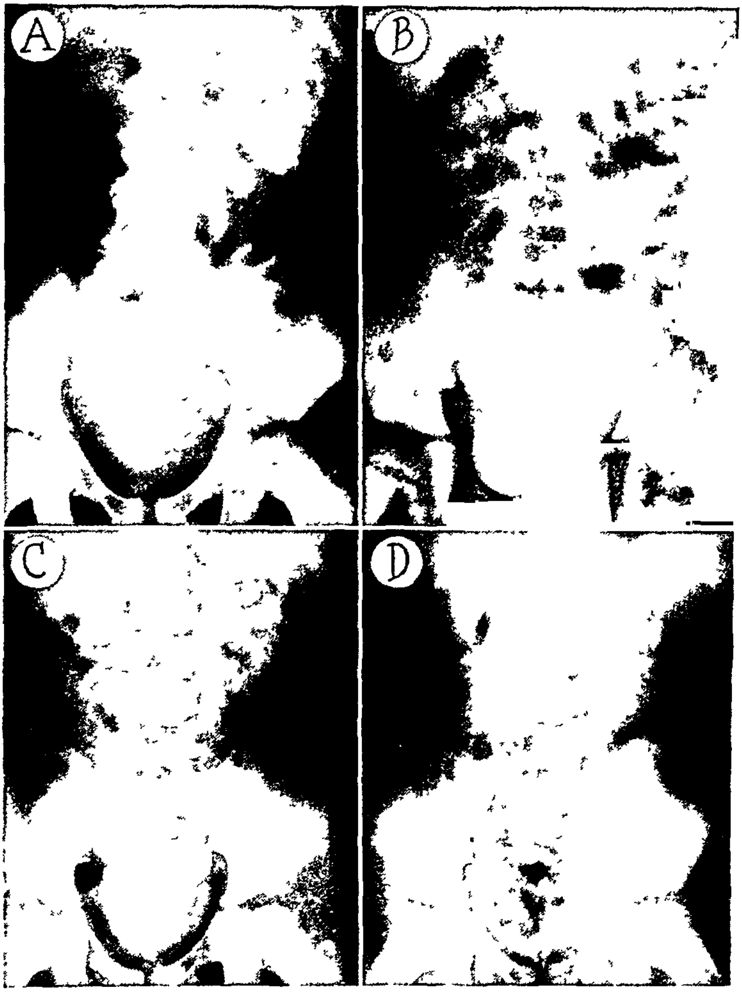

FIG. 8. Case 5. *A*, excretory urogram showing hydronephrosis and hydroureter. *B*, cystogram showing large diverticulum. *C*, 10-minute and *D*, 30-minute films of excretory urogram showing interval improvement 18 months after surgery.

pubic drainage. The child was transferred to Jefferson Hospital in October 1953 with chills, fever, suprapubic pain and purulent urine. The blood urea was 11.6 mg.; phenolsulfonphthalein output 40 per cent in 30 minutes; urine cultures revealed B. proteus and Esch. coli. The bladder capacity was reduced to 40 cc and the bladder spasms were almost continuous.

Figure 8, *A* and *B* show the initial excretory urogram and cystogram depicting left hydronephrosis, hydroureter and diverticulum of the bladder on October 6, 1953.

The infected urine was extremely resistant to the antibiotics. Subsequent sensitivity studies of the organisms to furadantin were favorable. With the use of this drug, beginning on January 20, 1954, improvement was finally realized.

On January 29, 1954, cystoscopy revealed an edematous, trabeculated bladder with numerous cellules and a diverticulum arising from the floor. The right orifice was not visualized even after indigo carmine dye injection. The left ureteral orifice was widely patent. There was a firm, fibrous contracture of the vesical orifice; in addition, a fold of fibrous tissue which began on the anterior lip at 2 o'clock and extended downward and forward to a point just proximal to the base of the verumontanum on the same side. Transurethral resection was carried out removing 1.5 gm. tissue. Following this the patient was observed to have a forceful stream of good caliber. Residual urine was measured at 20 cc.

On February 23, 1954, another gram of tissue (twenty pieces) was removed leaving little question as to the adequacy of the vesical orifice. The suprapubic tube was removed on March 10, 1954. Urine was free of infection and the residual was less than 5 cc. On March 15, 1954 the furadantin was discontinued after 55 days of continuous use and the patient sent home. He has received urethral dilatation at 2-month intervals since his discharge. The urethra now admits a 22F sound. The bladder capacity has progressively improved and is now 175 cc.

Figure 8, *C* and *D* show intravenous urograms in April 1955.

Comment: Again we see multiplicity of congenital abnormality both in the agenesis of the right upper urinary tract and a fibrous contracture of the vesical orifice. Prolonged suprapubic drainage was necessary here but the extremely resistant infection was the greatest difficulty at the onset. Furadantin was used with most gratifying results and no ill effect was observed in the 55 days of therapy. Revision of the original resection of the vesical orifice was necessary and one should not hesitate such repetition until the desired result is obtained. Our experiences concur with Burns et al. that vesical neck obstruction in children is more often due to congenital contracture rather than urethral valves. The method of approach in these cases is possibly better by the retropubic route than transurethrally. The difficulty with the small resector is a real problem. Exposing the prostatic urethra surgically is a very definite improvement and advance in the management of a greater majority of such lesions.

Case 6. L.N. was a white boy who, at the age of 2 months, was admitted to another hospital because of weight loss, vomiting, and diarrhea. Examination revealed a congenital aplasia of the penile urethra which barely admitted a No. 5 ureteral catheter. There was a prominent perineourethral fistula just above the anal margin through which he had passed urine since birth. The perineal fistulous tract was enlarged creating an external urethrostomy. During the following 4 years there was recurrent urinary tract infection and a vesicorectal fistula was suspected.

On July 3, 1950, the child was admitted to the Jefferson Hospital. Cystourethrography revealed a large bladder but no evidence of fistulous communication with the rectum, or reflux. Thirty cubic centimeters of methylene blue were instilled into the rectum and there was no trace of the dye in the urine during the following 24 hours. Excretory urography revealed a marked hydronephrosis and hydroureter on the left. Blood urea was 9.6 mg.; phenolsulfonphthalein output was 40 per cent in 30 minutes.

Cystoscopy revealed a trabeculated bladder with early cellule formation. The left ureteral orifice was easily identified in its normal position and appeared

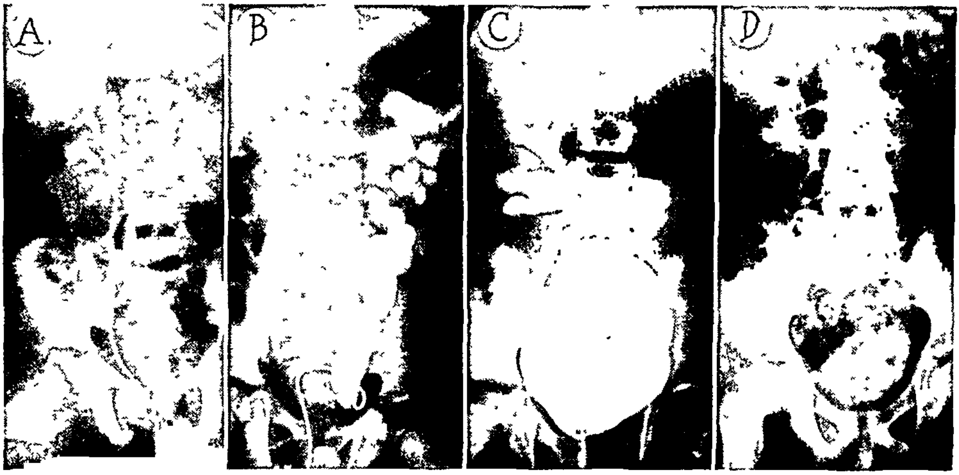

FIG. 9. Case 6. *A*, normal right retrograde pyelogram. *B*, marked left hydronephrosis and hydroureter. *C*, cystogram showing vesicoureteral reflux and hydronephrosis 5 years after surgery. *D*, excretory urogram showing improvement.

ovoid and patulous. The right ureteral orifice could not be identified so that 3 cc of indigo carmine dye was injected intravenously. After 3 minutes the dye was observed from the right ureteral orifice located on the posterolateral wall of the prostatic urethra 0.5 cm. from the vesical orifice. A No. 5 olive tip catheter was passed without obstruction. Differential phenolsulfonphthalein excretion was 8 per cent from the right and 5 per cent from the left in 15 minutes.

Figure 9, *A* and *B* show the right and left retrograde pyelogram in August 1950.

On August 28, 1950 a left nephrectomy and partial ureterectomy with cutaneous ureterostomy of the distal ureteral segment were accomplished.

On September 19, 1950 a No. 5 whistle tip ureteral catheter was placed to the right kidney through the ectopic orifice in the prostatic urethra. The bladder was then opened suprapubically and the vesical orifice and proximal portion of the prostatic urethra sufficiently exposed to see the ureteral catheter entering the right ureteral orifice. A grooved director was bent at right angles and inserted within the orifice and the ureteral catheter withdrawn. Using a hooked scalpel blade the bladder wall was opened from the ureteral orifice superiorly for a distance of about three centimeters. Several 5-0 chromic catgut sutures were placed to anchor the medial and lateral margins of the ureter thus exposed to the bladder mucosa. A No. 7 whistle tip ureteral catheter was passed to the right kidney and left indwelling. The distal segment of the left ureter was exposed and the left ureterectomy completed.

On June 12, 1951, exploration for the penile urethra was carried out. It was not found. Meatotomy of the perineal urethrostomy site was done and on September 27, 1951, the cystotomy tube was removed.

In November 1952, the child was readmitted because of urinary tract infection with B. proteus. A cystogram displayed reflux to the right upper tract with hydronephrosis. The condition is essentially unchanged, as shown by the cystogram and excretory urogram taken this year (fig. 9, *C* and *D*).

The child has remained free of symptoms since that time in spite of the vesicoureteral reflux. The perineal urethrostomy site is periodically dilated and antibiotic therapy has been necessary to combat recurrent episodes of infection. The blood urea is now 31.6 mg. and the phenolsulfonphthalein excretion 15 per cent in 30 minutes.

Comment: Our hopes to eventually attempt plastic reconstruction of the penile urethra have been diminished by the decrease in renal function. While we were pleased with one surgical effort in this case, the extensive right ureteral meatotomy designed to maintain the integrity of the only remaining kidney has created another serious problem. One wonders what the status of the right upper tract would be now if the orifice had been permitted to remain within the prostatic urethra. The question of reimplantation of the ureter has been discussed. Failure to reconstruct an adequate urethra has somewhat dampened our enthusiasm.

Case 7. D.K., an 8-month-old white boy, was admitted to the Jefferson Hospital on May 16, 1948 with exstrophy of the bladder. The child was nalnourished and suffered from chronic upper respiratory infection. Blood urea was 10.6 mg., CO_2 combining power 37 volumes per cent. On July 15, 1948, a right ureterosigmoid transplantation was carried out by the Coffey 1 technique.

On September 29, 1948, a left ureterosigmoid transplant was done by the same method. Blood urea 26.4 mg. and CO_2 combining power 39.5 volumes per cent at the time of discharge.

Figure 10 shows the excretory urogram before and after transplant.

On May 24, 1949, cystectomy and repair of the abdominal wall defect were accomplished. Blood urea 18.0 mg., CO_2 combining power 38.5 volumes per cent.

On June 13, 1951, plastic repair of the epispadias was done. Blood urea 22.8 mg., CO_2 combining power 36.6 volumes per cent. The child was readmitted on April 17, 1953, because of rectal bleeding and frequent bowel movements. Red

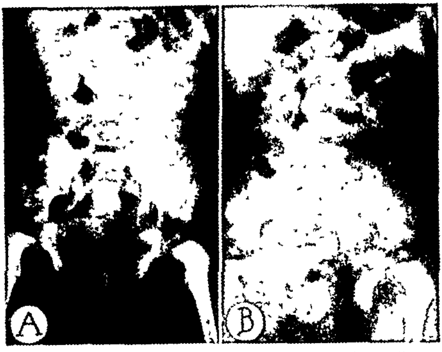

FIG. 10 Case 7 *A*, excretory urogram before and *B*, after bilateral ureterosigmoid transplant

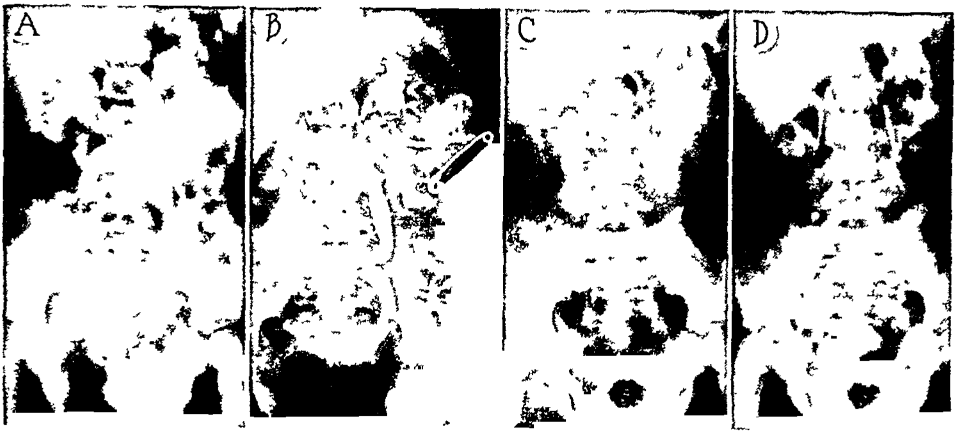

FIG. 11. Case 7. *A*, excretory urogram showing bilateral hydronephrosis 5 years after bilateral ureterosigmoid transplant. *B*, left antegrade pyelogram after nephrostomy and dilatation of anastomotic site. *C*, 5-minute and *D*, 10-minute films of excretory urogram 6 years after bilateral ureterosigmoid transplant.

blood cells 3.0 million; hemoglobin 54 per cent; blood urea 25.0 mg.; CO_2 combining power 30.9 volumes per cent. Excretory urography revealed early hydronephrosis with dilatation of both ureters, the left down to the ureterosigmoid junction and the right down to the pelvic brim. On May 15, 1953, a No. 28 panendoscope was passed into the rectum and indigo carmine injected intravenously. The right ureteral orifice was easily seen and a No. 7 whistle tip catheter was passed 15 cm. The left ureteral orifice could not be visualized. On May 18, 1953, a left nephrostomy was done during which procedure a No. 8 bulb catheter was passed antegrade from the renal pelvis through the ureterosigmoid anastomotic site. The child was given a blood transfusion and improved considerably. At the time of discharge the blood urea was 7.6 mg. and CO_2 combining power 45 volumes per cent. Figure 11, *A* shows the excretory urogram that reveals hydronephrosis and figure 11, *B*, the left antegrade pyelogram with reflux up the right.

The nephrostomy tube was removed in August 1954. The patient has continued to do well, has gained weight, and maintained a satisfactory red blood count. The blood urea was 25.0 mg. and CO_2 combining power 41.7 volumes per cent with plasma chlorides 614 mg. when seen in February 1955, some 6½ years after the transplant.

Figure 11, *C* and *D* show the intravenous urogram in August 1954.

Comment: This case displays both the complications of transplantation, rectoureteral reflux and stenosis of the anastomotic site. Fortunately, a period of nephrostomy drainage and antegrade dilatation of the left ureterosigmoid junction were sufficient to maintain renal function. It is also obvious that continued interest must be maintained in such cases in order to forestall a progressive renal insufficiency.

SUMMARY

Congenital malformations of the genitourinary tract in children with or without evidence of obstructive renal insufficiency require the most painstaking

interpretation before a course of therapy is activated. In general, the children we have treated fall into four catagories in regard to presenting symptoms: 1) and surely the most frequent group, those with recurrent urinary tract infection; 2) those with obstructive symptoms, namely, pain referable to the renal area or during the act of voiding; 3) and perhaps the most difficult to deal with, those who are chronically ill with associated anemia and symptoms referable to the respiratory and gastrointestinal tract; 4) those cases in which the child is asymptomatic and the urinary problem is an incidental finding either by the family or pediatrician.

It is rather interesting to note that in the greater majority of the defects noted in the external genitalia the upper urinary tract is peculiarly free of any evidence of gross disease or, indeed, malformation. Therefore, these cases do not present the problems which we have tried to stress in our presentation, unless complications should follow the reconstruction phase, which is not uncommon but they can be managed rather well today if one has the interest and perseverance to do so. On the other hand, the children with multiple obstructive lesions and the usual complicating features of such conditions promptly assume a formidable problem. It is this group of children who require the best of everyone concerned. If a sympathetic house staff is available many interlocking destructive complications may be obviated. Congenital lesions, if unilateral, with a competent renal system on the opposite side offer no great obstacle to successful management. If, however, it is incumbent to salvage both kidneys the area of error is much greater. The necessity of enrolling the help of everyone, including the family, is most essential.

CONCLUSIONS

The incidence of pediatric urologic disease is increasing in a general hospital population.

It is essential that pediatric urologic training be included in our residency program.

A group of illustrative cases of multiple, congenital obstructive lesions of the urinary tract in children has been presented with followup studies.

Adequate urinary drainage before any reparative procedure is carried out is fundamental.

Renal integrity must be maintained if satisfactory results are to be expected.

There is no doubt that the salvage rate in these children has increased due to many factors and not the least, the constant improvement in antimicrobic and chemotherapeutic agents.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

MECHANISMS OF HYDRONEPHROSIS: RADIOAUTOGRAPHIC BACKFLOW PATTERNS

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The recent contributions of Prather,[1] Frank Hinman Jr.[2] and Narath[3] have discussed the problem of the hydronephrotic kidney, and the possible routes of reflux of pelvic contents. The proposed pathways for this phenomenon include pyelovenous backflow,[4] pyeloglomerular backflow[5] and the pyelolymphatic form so frequently seen at the time of reflux attending retrograde pyelography. As a possible means of entering these channels in cases of obstruction, it has been further suggested that pyelotubular, pyelosinusoidal, pyelofornical or pyelointerstitial entrances exist.

Since all of the previous studies and discussions have failed to delineate the exact course of events in the obstructed kidney, attempts were made to utilize the more recent methods employing isotopic tracer materials. Our initial results, described previously,[6] showed that particles varying in size from ionic I^{131} to colloidal Au^{198} were able to gain access to the blood stream. This access was a rapid and ready one, and it was felt that a fairly direct shunt existed between the pelvis and the bloodstream. In an effort to more exactly outline this course, by tracing the radioactive material as it traversed the pelvic and renal mucosal barrier, radioautographic techniques were employed.

MATERIAL AND METHODS

Iodinated albumin was used in these experiments because of the relatively large particle size and the ease of counting and handling. Healthy mongrel dogs weighing between 10 and 15 kg. were employed. Under nembutal anesthesia, the ureter was exposed as closely as possible to the ureteropelvic junction and subsequently ligated about a specially designed needle (fig. 1, *A*) leading to a mercury manometer (fig. 1, *B*).

Under direct observation, without modifying the pressures as recorded on the attached manometer, a series of experiments was carried out in which the renal pelvic contents were replaced intermittently with the iodinated albumin. The routine dose ultimately employed to obtain satisfactory radioautographs was 5 millicuries. Ten animals were used in this study. After one hour the kidney

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Accepted for publication June 29, 1955.

Done in conjunction with facilities made available by AEC contract W31-109-eng-78 with Western Reserve University.

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was removed without ligatures being placed about the renal vessels on the kidney side, to allow drainage of blood from the renal vasculature. In five of the experiments, the pelvis was ligated at the termination of the experiment, and in the remaining five the pelvis was permitted to empty.

After surgical removal the kidney was placed in a freezing unit of the usual domestic type and permitted to remain there for a period of 24 hours to insure uniform hardness. At the end of this time the kidney was removed and sectioned coronally on a band saw. All cuts were made through the center of the kidney so as to bisect the renal pelvis and ureter when possible.

After section the kidney halves were prepared for radioautography in the following manner:

The cut surface of the section was covered with a thin layer of cellophane and was then approximated to a 4 by 5 inch photographic plate. The cellophane covered surface was held in close apposition to the emulsion by taping the kidney and glass slide tightly together. The slide and apposed kidney were then wrapped in a light-proof cover and were returned to the freezing unit for the duration of the exposure. The order of radioactivity employed in this experiment indicated an exposure period of about five to seven days, which proved entirely

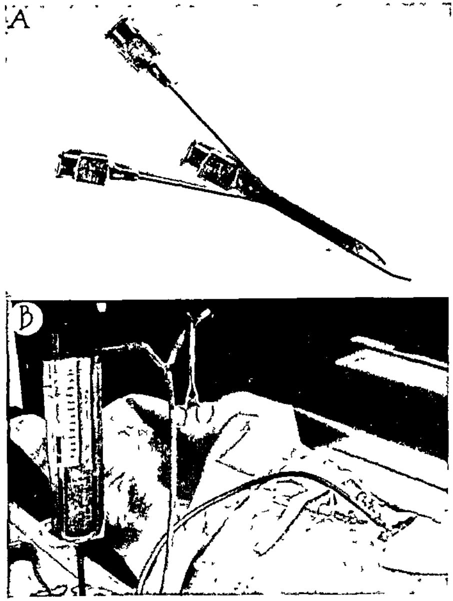

FIG. 1. *A*, [illegible]e with central cannula and fused hypodermic needles permitting [illegible] out modification of manometric pressure. *B*, experimental setup [illegible] to inflow and outflow syringes, and central cannula leading to easily read, sensitive manometer.

satisfactory. At the end of exposure the kidney sections were removed from the slides and discarded, and the slides were developed in the usual manner.

DISCUSSION AND RESULTS

Under the conditions of this experiment the backflow patterns were of two types. In figure 2, *A* and *B* are seen the patterns which we construe to mean pyelotubular backflow. This occurred in 2 out of the 10 cases. In figure 2, *C* and *D* are seen the second type of backflow, a combination of pyelotubular and pyelointerstitial. This occurred in the majority of instances, 8 out of 10, and was seen at the junction of the pelvic mucosa and the mucosal reflection covering the renal papilla (pyelosinusoidal). It is of interest that after the initial efforts in which inadequate amounts of radioactive material, less than five millicuries, were used and where the results were not interpretable, all of the results fall into one or the other of these patterns. The presence or absence of residual radioactive material in the pelvis did not modify the typical and predictable picture.

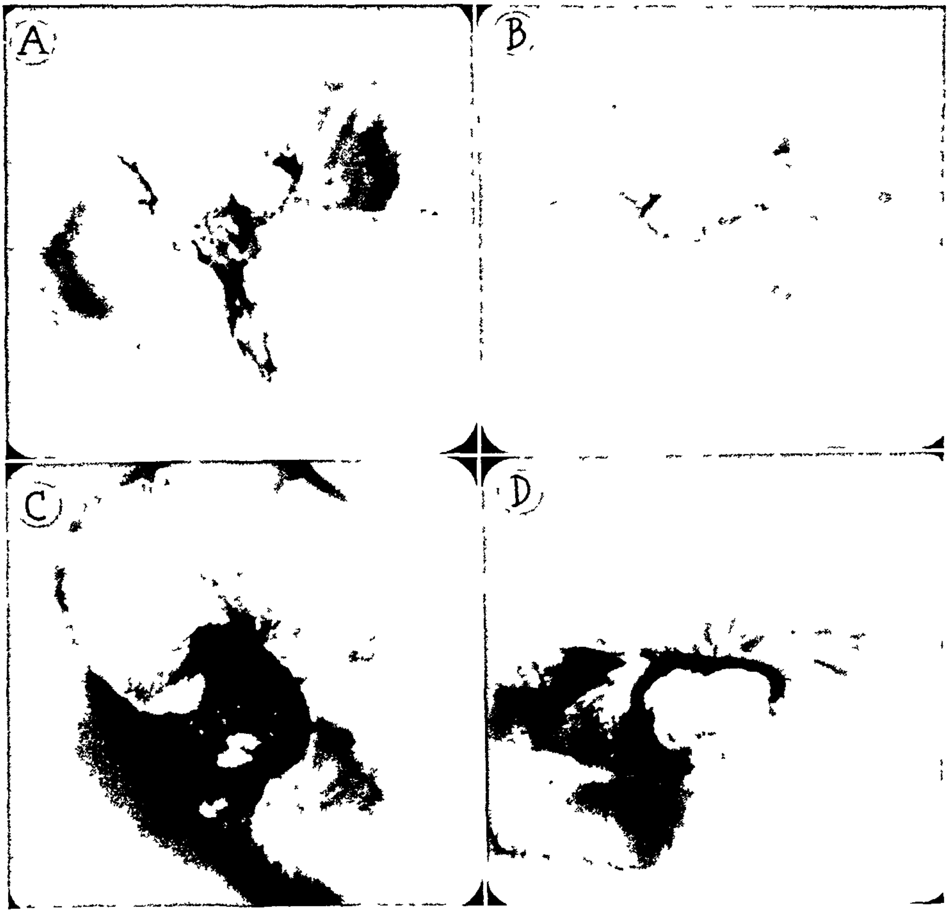

FIG. 2 *A*, radioautograph demonstrates pure pyelotubular backflow *B*, radioautograph demonstrates pure pyelotubular backflow, as in *A*. *C*, radioautograph demonstrates pyelotubular and pyelointerstitial backflow, latter occurring at junction of pelvic mucosa and mucosal reflection covering renal papilla Pelvic contents were in situ when frozen. *D*, pyelotubular and pyelointerstitial backflow, as in *C* except that renal pelvis was emptied prior to freezing

On inspecting these preparations one notes that where there was no fornical or sinusoidal backflow, the degree of pyelotubular extension was extreme and appeared to extend well toward the cortex; where there was associated pyeloformical absorption leading to pyelointerstitial reflux, the extension of the radioactivity up the tubules was minimal. The cause for this difference is not readily apparent. One possible explanation is that when reflux into the interstitial substance of the kidney occurs, the force causing pyelotubular backflow is diminished and limits the degree of its extension. In over distention created by manual pressure, Rolnick and Singer[9] noted mucosal tears at the fornices. Histological study of our kidneys did not reveal any anatomical derangement.

Whether these results can be exactly transposed to humans is of some question since, as has been pointed out by Hinman,[7] the anatomical pattern of the dog's kidney varies from the human. In the dog, as in a wide variety of experimental animals, there is only one papilla as compared to the multipapillary kidney of man with its columns of Bertin. Moreover, it has previously been observed that pyelotubular backflow is easily achieved in the dog. In man, it has been hypothesized[8] that this route of backflow is a late phenomenon, occurring after obstruction has persisted and dilatation taken place.

A further difficulty in completely translating these data to the human is the lack of reliable information concerning the normal pressure relationships in the human.[10] However, that these routes do occur in man has been suggested by Narath[4] as a result of fluoroscopic and roentgenologic visualization. Fuchs[5] *earlier had described pyeloformical backflow in human kidneys injected post-mortem.* We hope ultimately to reduplicate our own studies clinically when appropriate conditions present themselves. These experiments demonstrate that in the dog pyelotubular and pyelointerstitial routes of backflow occur early and that a rapid entrance into the blood stream is achieved, as manifested by the promptly demonstrable and mounting radioactivity in the peripheral blood. Particle size does not seem to influence this occurrence. By further investigation it is hoped that the main route for this backflow, whether pyelolymphatic or pyelovenous, can be determined. Certainly, in retrograde studies in the human, both routes are observed.

SUMMARY

In a series of 10 dogs, utilizing radioautographs, the route of backflow in acute hydronephrosis was seen to be a combination of pyelotubular and pyelointerstitial channels. No direct vascular shunt was demonstrated, although ready access to the bloodstream must be assumed by the rapidity of rise of radioactivity in the peripheral blood, as demonstrated in our earlier studies.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

PERINEPHRIC ABSCESS PRODUCING A PNEUMONEPHROGRAM

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Gas-forming infections in the upper urinary tract are rare if the paucity of case reports is an adequate criterion; but its serious import, when it does occur, warrants special attention to the importance of early recognition and treatment.

Reports concerning cases of pyelonephritis, pyelitis, renal cortical abscesses and postoperative wound infections are found in which gas-forming infections are noted, and these cases were mostly observed prior to the antibiotic era. No case of a gas-forming infection in the upper urinary tract extending into the perinephric tissue that caused abscess formation has been noted by the authors in the literature.

Some authors in the past have believed that the causative organisms producing gas in the urinary tract are anaerobic organisms, such as Bacillus aerogenes capsulatus (B. welchii, B. perfringens and B. capsulatus), vibrion septique and B. histolyticus. Other organisms that have been found in conjunction with those organisms are known to be gas-producing, but are believed to be secondary factors in the production of this condition in that they consume the oxygen which would otherwise prohibit growth of the anaerobe. However, we know that the common colon bacillus and others of the coliform group can produce gas just as they do from glucose bouillion in the incubator, and the majority of cases of gas infection in the urinary tract occur in diabetics whose cases are out of control. This explains part of the reason most of these gas cases yield only E. coli or other aerobic organisms on routine culture; the other being that anaerobes are not adequately cultured.

The following is an interesting case report of an extensive upper urinary tract infection in which gas formed in the renal and perirenal tissues:—

M. F., a white woman aged 60, entered the emergency room of a private hospital on February 11, 1954 in a state of coma. A history was obtained from the family. Three days prior to admittance, the patient had nausea, vomiting and some vague abdominal pain. These symptoms persisted and the patient ate nothing. She gradually became comatose 2 hours prior to admission. She was not a known diabetic and had no past history of convulsions. No note was made either of sedatives being taken, or trauma.

Physical examination revealed an obese, comatose patient who responded only to painful stimuli. The skin was warm and dry and the temperature was 105F rectally. The blood pressure was 40/20 and pulse 108. The remainder of the physical examination was essentially negative except for a few moist rales in the left lung base, and pain on palpation of both upper abdominal quadrants.

The patient was admitted to the hospital and was given oxygen, antibiotics and intravenous fluids. These methods of treatment were carried out for the

Accepted for publication July 20, 1955.

next 18 hours and the blood pressure rose to 130/70 and the rectal temperature dropped to 101F. Blood sugar drawn about this time was over 600, nonprotein nitrogen 68 and chlorides 83 m/Eq. It was evident that the patient was in diabetic coma and, accordingly, insulin was given, as was intravenous lactate, Ringer's and normal saline solutions. The urine at this time showed acetone and glycosuria.

On the aforementioned regimen, the patient responded rapidly and in 2½ days was out of coma, alert and able to answer questions. The blood sugar was lowered to 280 and a diabetic diet was started.

A chest film on the second hospital day showed the left leaf of the diaphragm to be obscure due to a density in the base of the left chest. A re-check chest film showed the same as the first film, the density being interpreted as fluid and questionable air under the left diaphragm. A portable flat x-ray that was taken of the abdomen showed free air in the perirenal area and also in the parenchyma of the left kidney (fig. 1, *A*). The patient's physician considered the possibility of a bronchopleural-retroperitoneal fistula.

By February 19, the patient was up and about. Re-examination of the abdomen showed an increase in the amount of air around the left kidney and within the kidney substance (fig. 1, *B*). On February 21, an increase in the air pattern was noted in the left renal area (fig. 1, *C* and *D*). Ten days after admission, urologic consultation was obtained. Excretory urography showed a nonfunctioning left kidney. Cystoscopy revealed a normal bladder with grossly cloudy urine. A catheter was passed to the left kidney with much difficulty and purulent urine was obtained. A retrograde pyelogram showed dilatation of the left ureter and pelvis with extravasation of dye out into the soft renal parenchyma (fig. 1, *E*). The right upper tract was normal and clear urine was obtained from the right kidney. Urine culture from the bladder and left kidney showed E. coli and Aerobacter aerogenes, very sensitive to furadantin and terramycin. The bacteria produced gas on inoculation into culture tubes. The blood sugar at this time was leveling from 200 to 300, but never lower.

The medical service was very hesitant to see the patient operated on but, in view of the inability to further lower the blood sugar and the increasing size of the renal air pocket and the perirenal air outline, an operation was scheduled March 1, 1954. A regular left flank renal incision was made. As soon as the perinephric area was entered, a gush of gas came out followed by a large amount of thick, creamy pus. The blood pressure dropped precipitously. Palpation of the left kidney revealed it to be crepitant and the pedicle felt friable. The kidney seemed to be lying free within the space. Because of the patient's condition, the kidney was not removed. Many drains were placed into the area and the wound packed open.

On the second postoperative day, the blood sugar level was 118. Culture obtained from the perinephric abscess revealed E. coli and Aerobacter aerogenes. These bacteria produced gas on inoculation into the culture tubes. A large amount of pus drained from the abscess area and frequent re-dressings were required. The urine soon became free of sugar and acetone for the first time. The

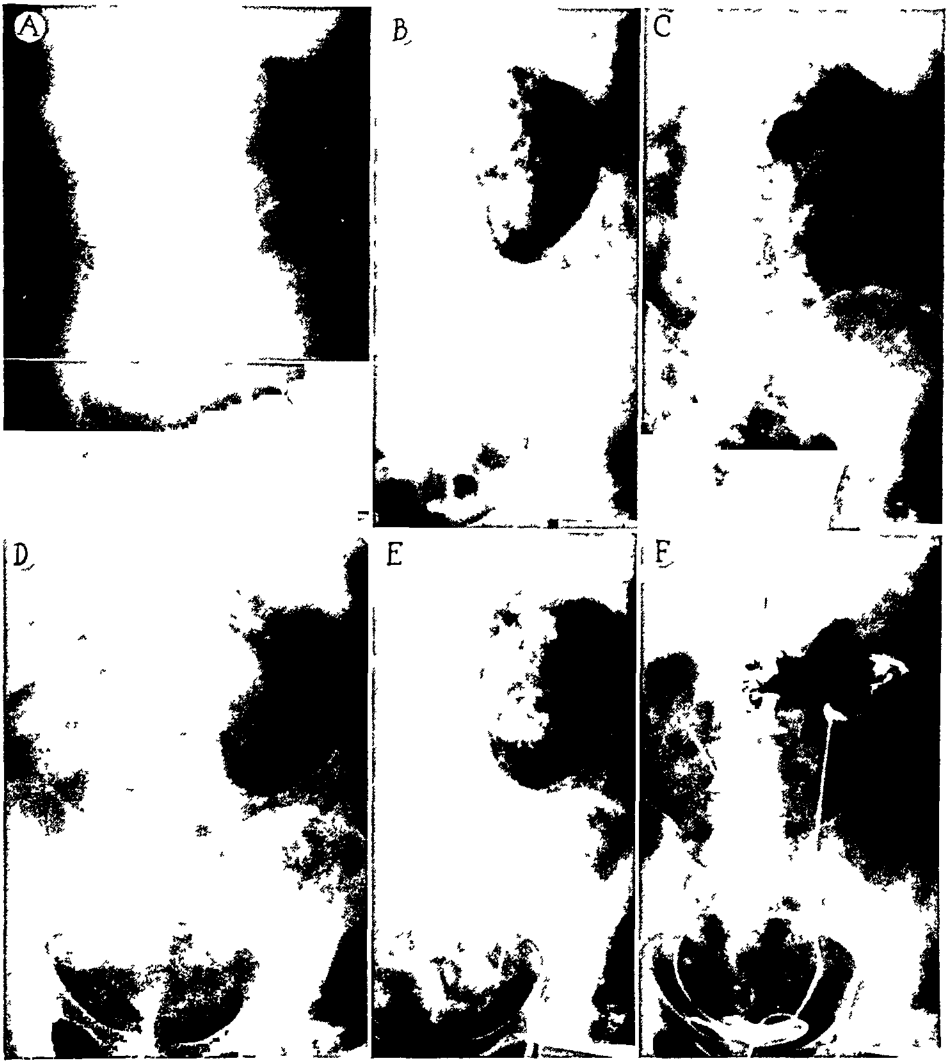

FIG. 1. *A*, film taken while patient was comatose and diagnosis still in process of being made *B*, film of abdomen taken after patient's diabetes had been controlled to extent that she no longer was in coma. *C*, film 6 days after that depicted in *A* had been taken. Note increased size of perirenal shadow. *D*, film 2 days after that depicted in *C* had been taken. Note progression of perirenal air shadow and, in addition, linear lines of air corresponding to renal parenchyma *E*, retrograde pyelogram showing marked extravasation of skiodan into soft renal parenchyma *F*, retrograde pyelogram taken many months after operation. Blunt end of upper ureter and extravasation were suggestive of absent kidney. (Kidney may have sloughed away during period of drainage)

patient rapidly improved during the ensuing weeks; the drainage from the wound gradually became minimal and the wound healed slowly. The patient's insulin requirements finally became only 10 units protamine zinc insulin each morning.

By October 1954, the wound had healed completely, and the patient was feeling very well. Urine culture showed E. coli again with the same sensitivity. Retrograde pyelography was repeated in the fall of 1954. The catheter was passed up the ureter and skiodan injected. The dye seemed to extravasate out into the tissues. There was no renal outline (fig. 1, *F*). It is the assumption of the writers that probably the left kidney sloughed out By February 1955, the patient was feeling well and no longer taking insulin The urine revealed pus cells and E coli on culture, but the patient was free of urinary symptoms

SUMMARY

A rare case report of a gas forming perinephric abscess and a severe upper urinary tract infection with gas formation has been presented The patient, unknown to have diabetes, became comatose Severe upper urinary tract infection, caused by E coli, developed with the production of gas in the collecting system and extended into the perirenal tissues Thus, a typical perinephric abscess was formed The patient's diabetic condition did not respond to the fullest extent until the perinephric abscess was opened and drainage established That the severe infection destroyed the kidney completely was evident from followup films Nature did what it was impossible to do at surgery remove the infected kidney

Certainly this condition, even though uncommon, must be considered when an infected urinary tract shows evidence of gas in the renal area—parenchyma or perirenal tissue More often it is seen in diabetic patients, and not always will an anaerobic organism be responsible In fact, more frequently E coli and/or Aerobacter aerogenes will be present Antibiotics, supportive therapy and surgical drainage of the renal area are the choice and indicated means of therapy

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THE JOURNAL OF UROLOGY
Vol. 75, No 2, February 1956
Printed in U S A.

A LOW LYING LEFT KIDNEY

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Most anatomy texts in defining the position of the kidneys state that the right kidney is lower than the left, possibly because of the position of the liver. The physician whose duties include the evaluation of large numbers of pyelograms frequently observes the opposite to be true and is therefore faced with the responsibility of assessing the clinical significance of this phenomenon.

In an effort to ascertain incidence of cases in which the left kidney is lower than the right, 1,500 consecutive excretory urograms were reviewed, and the left kidney was found to be lower in 106 cases or 7.1 per cent. A study was then made of the 106 cases in an effort to establish a reason for this anatomical deviation. It was found that in 29 instances the low-lying left kidney could probably be attributed either to a specific disease entity or to an anatomical abnormality, as indicated below.

A. Intrinsic (fig. 1, *A*)	
Calculus, staghorn	1
Pyelonephritis	9
Hydronephrosis	3
Renal cyst	2
B. Extrinsic (fig. 1, *B*)	
Adrenal cortical adenoma	2
Neuroblastoma	2
Abscess, perinephric	3
C. Anatomical (fig. 1, *C*)	
Scoliosis	2
Situs inversus	1
Renal ectopia	4
Total cases	29

In 77 cases no explanation could be found to account for the position of the left kidney, and it was therefore concluded that the left kidney was "normally" lower than the right in 5.1 per cent of the 1,500 cases.

On reviewing the medical records of these 77 patients, however, it was found that 40 (51.9 per cent) had blood pressure values within the hypertensive range (fig. 1, *D*). The high incidence of hypertension among patients in this study may in part be accounted for by the incidence of hypertension in the general population, estimated to be somewhere between 25 and 40 per cent,[1, 2] and also that approximately 10 per cent of all excretory urograms made at the University Hospital are made solely in the effort to determine a possible renal cause for the hypertension. Nevertheless, when a downward displaced left kidney is found in association with hypertension, investigative procedures are indicated to rule out an adrenal tumor.

Accepted for publication July 20, 1955.

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In summary, it was found that the left kidney was lower than the right kidney in 7.1 per cent of 1,500 cases reviewed. The significance of this finding is twofold: First, the high incidence of known pathological entities; and second, the remote possibility of an adrenal tumor manifested clinically by hypertension only.

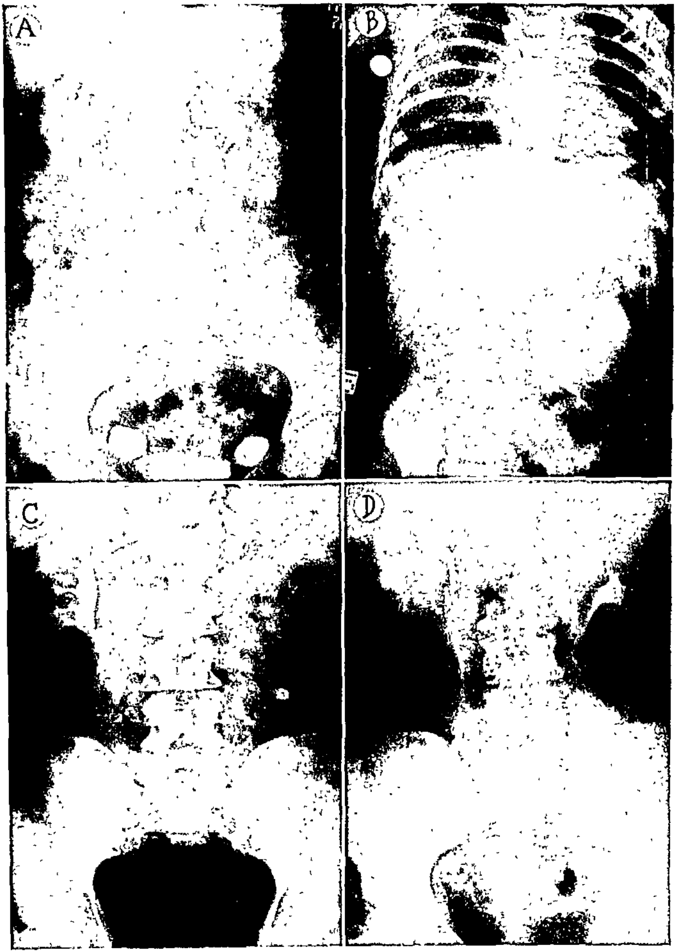

Fig. 1. *A*, left kidney displaced downward by upper pole renal cyst. *B*, large retroperitoneal neuroblastoma was found displacing downward normal left kidney. *C*, left renal ectopia. *D*, normal excretory urograms in 57-year-old woman. Blood pressure 230/120

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

INTRINSIC RENAL FUNCTION

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This paper was designed to make available to the interested reader a brief and quickly comprehensible analysis of the processes involved in urine formation and how they are currently used to measure renal blood flow and to indicate the extent to which the different parts of the nephron may be involved.

Two chief processes are active in the formation of urine from normal blood, namely, filtration and resorption. Filtration means the passage of filtrable substances from the blood plasma via the glomeruli into the nephrons as a result of a hydrostatic pressure in the glomerular capillaries in excess of the colloid osmotic pressure of the plasma. Since filtration thus defined is peculiarly renal and glomerular, it is superfluous to say "glomerular filtration" or to use other qualifying words or phrases.

The use of inulin as a substance generally regarded as being solely filtered and not subsequently resorbed, has supplied a means of determining the rate and amount of filtration and the total plasma flow. To measure such flow, the clearance of inulin is divided by the plasma extraction ratio of inulin, i.e., inulin's renal venous concentration divided by its renal arterial concentration. Of substances used in this connection, it does not appear that variations in clearances or in plasma extraction ratios make significant differences in the determination of renal plasma flow by the indicated division. The average inulin clearance is 130 ml. per minute and the average plasma extraction ratio is 0.20. This clearance divided by this extraction ratio gives a renal plasma flow of 650 ml. Such flow approximates closely the plasma fraction of the total volume of blood estimated to pass through both kidneys per minute, namely, 55 per cent of 1200 ml.

If the total renal plasma flow is 650 ml. as determined by the excretion of a substance solely via the glomeruli, what is this flow when determined by the excretion of a substance chiefly or solely by the nephrons—the so-called renal tubular excretion? The preferred substance in this connection is para-aminohippurate (PAH). Its average clearance is 630 ml. and its plasma extraction ratio is best taken as 0.92. This ratio means that clearance is almost complete during one circulation. A clearance of 630 ml. divided by an extraction ratio of 0.92 gives a renal plasma flow of 685 ml. per minute. Of this amount 8 per cent (55 ml.) can be regarded as distributed to nonexcretory renal tissue (Smith,[1] p. 163) and 15 per cent (94 ml.) as cleared by filtration. Thus, 536 ml. of the total renal plasma flow are cleared by the nephrons. But it is only the proximal convolutions (miscalled "proximal tubules") which comprise 40 per cent of the average total length of the nephrons, that are involved in this clearance of PAH. Therefore, the distribution of blood to these convolutions should be considered. Since most of the

Accepted for publication July 28, 1955.

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[1] Smith, H. W.: The Kidney: Structure and Function in Health and Disease. New York: Oxford University Press, 1951.

blood leaving the glomeruli is continuously available to the proximal convolutions, their surface area and the speed of transport of substances across their walls are primary factors in the clearance of substances by them In the functioning kidney their surface area should amount to 70 per cent of the total surface area of the nephrons since in the fixed kidney their surface area amounts to 60 per cent This area is adequate for the clearances that have been determined by various investigators The tabulation below is given as inclusive of what should be considered in measuring renal plasma flow by the clearance and extraction ratio of PAH

6000 ml —cardiac output per minute
1200 ml —20 per cent of the cardiac output to both kidneys—the renal fraction
660 ml —55 per cent of 1200 ml as plasma
630 ml —average clearance per minute
685 ml —renal plasma flow per minute as determined by dividing a clearance of 630 ml by an extraction ratio of 0 92
536 ml —plasma cleared per minute by the proximal convolutions
94 ml —plasma assumed to be cleared per minute by the glomeruli (filtration clearance)—72 per cent of the simultaneous inulin clearance of 130 ml , this being the per cent of filtrable PAH available

The renal plasma flow as measured by the clearance and extraction ratio of phenolsulfonphthalein (PSP, phenol red) is given here for comparison with that of PAH It is established that PSP is excreted chiefly—perhaps solely—by the proximal convolutions, whereas a like excretion of PAH is less well known However, there is no basis for believing that PAH or any substance passing from perinephronic blood to the lumens of the nephrons does so by other subdivisions of the nephrons than their proximal convolutions In the tabulation below (see Smith,[1] p 274) the average clearance of PSP is much less than that given above for PAH No satisfactory explanation is available concerning this difference It is surmised that it may be the result of the high per cent of PSP that is bound to the albumin of the plasma or to some limitation in its mode of transfer across the walls of the proximal convolutions

402 ml —typical clearance per minutes
730 ml —renal plasma flow per minute as determined by dividing a clearance of 402 ml by an extraction ratio of 0 55 This is 60 per cent less than the extraction ratio of PAH
379 ml —plasma cleared per minute by the proximal convolutions
23 ml —plasma considered as cleared per minute by the glomeruli (filtration clearance—20 per cent of the simultaneous inulin clearance of 115 ml , this being the per cent of filtrable (unbound) PSP available during the clearance determinations

In the preceding tabulations the clearance of PAH and PSP via the glomeruli is given as 94 and 23 ml , respectively Such filtration clearances are said to be contingent upon the fractional binding of these substances to the plasma albumin The unbound fraction, which varies with the concentration of the substance in the plasma, is filtrable. If at a given concentration it amounts to 30 per cent of the total, then its glomerular clearance, it is assumed, will be 30 per cent of the simultaneous inulin clearance. But it has not been proved that partly filtrable substances are filtered only to the extent of their filtrability or that completely filtrable substances are excreted solely via the glomeruli. The latter have been shown to be excreted simultaneously by the glomeruli and nephrons. Also, it is the unbound (filtrable) fraction of a partly bound substance that is excreted by the proximal convolutions. This fraction passes across the walls of adjacent capillaries to surround these convolutions. This occurs in proportion to its availability by dissociation from the bound fraction accompanying its removal from the plasma.

Glomerular and nephronic excretion involves two different sites and modes of transfer. It is known that filtration depends on an excess of hydrostatic over colloid osmotic pressure in the glomerular capillaries, but it is not known what obtains in the clearance of substances by the nephrons. The renal blood flow and perhaps volume seem determinable in connection with clearances either by the glomeruli or the nephrons. Clearance by the latter is accomplished by their proximal convolutions. These comprise 40 per cent of the total length of the nephrons and 60 per cent of their surface area when they are inactive. Information concerning the functional status of these convolutions may be obtained by the clearance of PAH, PSP and diodrast, but not concerning other parts of the nephron.

RESORPTION

An important aspect of renal functioning is revealed in the resorption or return to renal blood or lymph of variable amounts of those constituents of plasma that have gained access to the lumens of the nephrons. Where and how within the nephrons this resorption occurs, is not adequately known—especially in the mammalian kidney. As regards the latter and as a result of certain experiments performed on guinea pigs and rats,[2] a basis was supplied for believing that most of the resorbed water and solutes are resorbed from the proximal convolutions. An analysis of these experiments may indicate whether or not this basis is valid. The animals were first unilaterally nephrectomized and variably later (5–43 days) a given animal, in an extreme state of induced diuresis, was subjected to the following procedure: The remaining kidney was exposed and a capillary pipette containing a thin, colored oil was inserted into the lumen of the proximal convolution and the oil released. When the oil became static after it had been carried variably distal to the pipette by fluid from the glomerulus, withdrawal of fluid for analysis was begun. It was believed that only fluid from that part of the lumen proximal to the oil was collected. By tapping a given convolution at various levels (level determined after the experiment) it was found that the analyzed constituents in the collected fluid, namely, glucose after phlorhizin, exogenous creatinine, and chloride, were progressively concentrated the more distant from the glomerulus the fluid was collected. The explanation offered for this increased concentration was that approximately 80 per cent of the water was resorbed by the time the fluid leaving the glomerulus reached the terminal portion of the proximal convolution. Nevertheless, the fluid collected from this convolution was found to be isosmotic with plasma. This made it necessary to postulate the resorption of an osmotically active solute along with the water in order to maintain this isosmotic relation.

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[2] Walker, A. M., Bott, P. A., Oliver, J. and MacDowell, M. C.: The collection and analysis of fluid from single nephrons of the mammalian kidney. Am. J. Physiol., **134:** 580, 1941.

The validity of these experiments depends largely on whether the injected oil constituted an effective block to the back passage of fluid distal to the oil. The authors believed that it did despite the following: 1) The oil, although said to be static, was in continuous "pulsatile movement." This of itself would indicate that back passage of fluid distal to the oil was possible. Also, in 9 of 59 experiments, the injected oil, after it had been carried a short distance away from the pipette, rushed suddenly back to the pipette and out through the puncture, thus forming, with the accompanying fluid, a blister beneath the renal capsule. This fluid was collected and analyzed and the analysis was incorporated in the published data. 2) The indifferent contact of the oil with the brush border, which lines the inside surface of the convolution, could have permitted the back passage of fluid distal to the oil into the part from which fluid was being withdrawn (fig. 1, sketch at right). Such passage was likely facilitated by the length of time (20 or more minutes) that was required in order to collect enough fluid for analysis—especially when fluid was being withdrawn from the more distal parts of the convolution where the greatest increase in concentration of the analyzed constituents

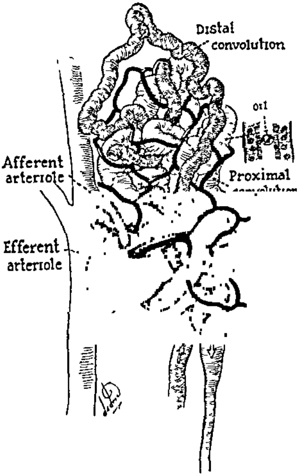

FIG. 1. Diagrammatic representation of distribution of capillary blood to proximal and distal convolutions of a nephron. Proximal convolution is responsible for excretion of para-am [illegible], at right of figure, sketch of segment of [illegible] be in its lumen when used to block back pa[illegible]

occurred. 3) It is from the segments continuous with the proximal convolution (thin segment and ascending limb of the loop of Henle) that marked resorption of water occurs but without indication of the simultaneous resorption from these segments of significant amounts of solutes—especially chloride. Therefore, the nonresorbed solutes would become more concentrated. When they are drawn back into the lumen of the proximal convolution and thereby comprise a part of the collected fluid, this would account for the progressive increase in concentration of the constituents in the fluid collected from the more distal levels of this convolution.

Whatever may be the situation with regard to the resorption of glucose and amino acids from the proximal convolution, there is no reliable evidence that considerable amounts of water and electrolytes are resorbed from it. Other segments of the nephron have been shown to be primarily active in this connection.

UREA

This substance is believed to be solely filtered. Its average clearance is approximately 55 per cent of the average, simultaneous inulin clearance. The tabulation below, based on data given by Smith,[1] p. 44, shows significant aspects of such clearances when both are considered as filtered but without the resorption of inulin. Noteworthy in the tabulation is the amount of urea (40 per cent, Smith, p. 72) believed to be resorbed "passively" (by diffusion) from the proximal convolution of the dog's kidney because of the progressive concentration of the fluid in the proximal convolution from a creatinine U/P ratio of 1.0 to a U/P ratio of 8. At an inulin U/P ratio of 8 in man the same amount of urea resorption is believed to occur as in the dog's kidney. Smith, p. 72, says: "Throughout the entire range of urine flow it is permissible to interpret the deficit in urea clearance as the result of passive diffusion of urea somehow related to the degree of concentration of the tubular urine and hence to the diffusion gradient of urea between the tubular urine and the blood and the time available for diffusion."

0.24 mg.	inulin per ml. of plasma.
0.21 mg.	urea per ml. of plasma.
136.00 ml.	plasma cleared of inulin.
75.00 ml.	plasma cleared of urea (55 per cent of the inulin clearance).
33.00 mg.	inulin excreted (136 ml. × 0.24 mg.).
15.75 mg.	urea excreted instead of 28.56 mg. that would be excreted if no urea were resorbed (75 ml. × 0.21 mg. instead of 136 ml. × 0.21 mg.).
12.81 mg.	urea resorbed (28.56 mg. minus 15.75 mg.).
11.42 mg.	urea believed to be "passively" resorbed from the "proximal tubule" (40 per cent of 28.56 mg.).
1.39 mg.	urea believed to be resorbed from the "distal tubule" (12.81 mg. minus 11.42 mg.).

From the preceding it can be seen that if urea is solely filtered, then 45 per cent is resorbed. Its resorption from the "proximal tubule" amounts to 89 per cent of the total urea resorbed (89 per cent of 12.81 mg.) and is believed to be the result of "passive diffusion" occurring at the same time as the "passive reabsorption" of 84.6 per cent of the filtered plasma water—chiefly also from this tubule. An "active reabsorption" (under hormonal control) of the remaining 14.6 per cent of such water is stated to occur from the "distal tubule." This requires that of the available 136 ml. of water, 115 ml. were resorbed chiefly from the so-called proximal tubule and 18.3 ml. from the so-called distal tubule, thus leaving 2.7 ml. to be excreted as urine.

Whether or not the amount of urea and water resorption can occur from the proximal convolution, as indicated above, is indeed doubtful. It is also doubtful whether urea or any resorbed substance is returned to renal blood as a result of diffusion regardless of its diffusibility, molecular weight, or peculiar conditions of concentration that may obtain within the lumen of the nephron. In support of this doubt is the disparity between the diffusion coefficients, molecular weights, the sites and degrees of resorption, if any, in these sites of such substances as urea, creatinine, ferrocyanide, electrolytes, glucose, phenol red and PAH.

SODIUM

The evidence appears conclusive that sodium and chloride are eliminated from plasma by filtration alone. Their clearance shows that they are resorbed in large amounts following their filtration. As regards sodium it is believed (Smith, p. 326) that approximately 80 per cent is "actively" resorbed, i.e., against a concentration gradient, from the lumen of the proximal convolution concomitantly with the "passive" resorption (diffusion) of 85 or more per cent of the filtered water (Smith, pp. 243, 311). Although the sodium ion is highly diffusible, nevertheless, it is said to be resorbed against a concentration gradient while urea, under similar conditions, is said to be resorbed as a result of "passive diffusion." Smith's view is that most of the substances that are in process of excretion are resorbed from the proximal convolution in varying amounts accompanied by the resorption of 85 or more per cent of the filtered water. If this were correct, casts would commonly form in the lumen of the proximal convolution. This does not occur. Also, this convolution is the first subdivision of the nephron. It receives all the filtrate from the glomerulus. Therefore, the flow through its lumen should be more rapid than that through the lumen of succeeding subdivisions. Such rapidity would not be permissive of the massive resorption that is believed to occur. Moreover, critical examination of the density of substances such as ferrocyanide, uric acid, and hemoglobin that have been precipitated in the lumen of the proximal convolution when the kidney was fixed during their excretion, does not suggest the resorption of significant amounts of water. There is not (as is claimed) that progressive increase in the density of the precipitated substance, beginning at the glomerulus and continuing through this convolution, that would indicate such resorption.

The tabulation which follows will serve to show the relationship between inulin and sodium clearance and sodium resorption when both inulin and sodium are simultaneously filtered.

0.24 mg. inulin per ml. of plasma.
3.25 mg. Na per ml. of plasma.
3.50 mg. Na per ml. of urine.

136.00 ml. plasma cleared of inulin per minute.

1.18 ml. plasma cleared of Na per minute at an average urine flow of 1.1 ml. per minute (3.5 mg. Na per ml. of urine × 1.1 ml. urine flow divided by 3.25 mg. Na per ml. of plasma).

3.84 mg. Na excreted per minute (3.25 mg. Na per ml. of plasma × 1.18 ml. of plasma cleared of Na).

438.16 mg. Na resorbed (442.00 mg. Na in 136 ml. of filtrate minus 3.84 mg. Na excreted per minute—99 per cent resorbed).

350.00 mg. Na resorbed from the proximal convolution (80 per cent of 438.16 mg.—Smith[1]).

88.00 mg. Na resorbed from the distal convolution (438.16 mg. minus 350.00 mg. Na).

AFFERENT AND EFFERENT ARTERIOLES

Maintenance of the rate of filtration during a reduction in renal blood flow as well as variations in the amount of filtration are commonly attributed to differential vasomotor changes in these arterioles. Also, certain increases in filtration not attributable to other factors are said to be due to a constriction of the efferent arteriole alone. This may be an actual or relative constriction.

Views concerning the intrinsic regulation of glomerular blood pressure and blood flow are traceable to the work of A. N. Richards and his collaborators.[3-7] It is explicit in this work that the efferent arteriole, under certain conditions, may constrict more than the afferent or independently of the latter and also that if both arterioles constrict simultaneously and to the same degree, the efferent arteriole will be more effective in increasing glomerular capillary pressure. The reason given for such effectiveness was that the efferent arteriole is smaller than the afferent and therefore a vasoconstrictor acting alike on both would produce a greater increase in resistance to blood flow in the smaller vessel.

Another possibility was given by Richards but is rarely if ever cited, namely, that glomerular pressure may be altered by a differential action of vasodilators on the afferent and efferent arterioles. A filtrable vasodilator in the blood passing through the glomeruli will be filtered in part and thus reduce the amount available for action on the efferent arteriole. Accordingly, the intraglomerular pressure will rise since the efferent arteriole remains relatively constricted. Although in the kidney of the living animal (frog) neither arteriole could be seen to constrict or dilate, the glomerular tuft was seen to increase in size when minute amounts of adrenalin were added to blood and the kidney was perfused with it. The per-

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[3] Richards, A. N.: Kidney function. Am. J. Med. Sci., **163:** 1, 1922.

[4] Richards, A. N. and Plant, O. H.: Urine formation in the perfused kidney. The influence of adrenalin on the volume of the perfused kidney. Am. J. Physiol., **59:** 184, 1922.

[5] Richards, A. N. and Schmidt, C. F.: A description of the glomerular circulation in the frog's kidney and observations concerning the action of adrenalin and various other substances upon it. Am. J. Physiol., **71:** 178, 1924.

[6] Richards, A. N.: The nature and mode of regulation of glomerular function. Am. J. Med. Sci., **170:** 781, 1925.

[7] Richards, A. N., Barnwell, J. B. and Bradley, R. C.: The effect of small amounts of adrenalin upon the glomerular blood vessels of the frog's kidney perfused at constant rate. Am. J. Physiol., **79:** 410, 1927.

fusion was exclusively renal in order to avoid invalidating effects that could obtain if the heart and other than renal vessels were involved.

The preceding constitutes the basis for the commonly held view that differential constriction of the efferent arteriole is responsible for a variety of phenomena manifest in connection with changes in or regulation of glomerular capillary pressure, glomerular blood flow and rate of filtration. The most direct evidence of such constriction is afforded by the cited increase in size of the glomerular tuft thereby indicating active constriction of the efferent arteriole without appreciable change in the afferent. Nevertheless, it is difficult to believe that a differential constriction of the efferent arteriole occurs because of other facts in this connection. These facts are: 1) In the human kidney, precise measurements have been made of the diameters of the lumens of efferent arterioles in the cortex peripheral to a narrow, juxtamedullary zone. They are the same as or one micron smaller than those of associated afferent arterioles. 2) In the juxtamedullary zone, efferent arterioles that descend into the medulla (at least 15 per cent of the total number of such arterioles per kidney) have lumens that are two or more microns larger than those of associated afferent arterioles. Therefore, a vasoconstrictor acting equally on both types of arterioles would not reduce the lumens of efferent arterioles in the peripheral cortex appreciably more than those of similarly located afferent arterioles. Efferent arterioles that descend into the medulla would still have lumens two or more microns larger than those of associated afferent arterioles.

Of interest here also, is the fact that the media of the wall of afferent arterioles in the peripheral cortex (85 per cent of the total number of such arterioles per kidney) is approximately one-third thicker than that of similarly located efferent arterioles. A vasoconstrictor acting on such media would certainly be limited by the amount of available smooth muscle composing such media. Therefore, the thickness of the media as well as the size of the lumen of afferent and efferent arterioles should be considered in connection with the regulation of glomerular blood pressure and blood flow. The walls of afferent and efferent arterioles in the juxtamedullary zone have approximately the same thickness but the lumens of most of the efferent arterioles in this zone are larger than the afferent.

It is not known in requisite detail how glomerular blood flow and pressure are regulated and no method is as yet available whereby they can be reliably tested. It appears likely that the glomerular capillaries, the efferent arterioles and the capillaries arising from them are simultaneously *involved in changes in glomerular* activity not correlatable with changes in afferent arterioles.

TERMINOLOGY

In normal kidney function, blood plasma is ultrafiltered via the glomeruli and the filtered constituents are resorbed in variable amounts en route through the lumens of the nephrons. Thus, filtration and resorption appear to be the chief processes known to be primarily involved in normal urine formation. Certain substances that are not normal constituents of blood can pass readily from blood across the wall of the nephron to its lumen. Such passage might well be designated as extraction. Then the terms filtration, resorption and extraction would signify all that is or could be directly involved in urine formation. It would not be necessary to speak of glomerular filtration, tubular resorption and tubular excretion. The use of "tubular" in connection with the passage of substances to or from the lumens of nephrons seems redundant since such passage can only be tubular.

SUMMARY

Simplified and comprehensive data are given concerning the renal plasma flow as measured by the clearance and plasma extraction ratio of a substance, inulin, that is believed to be cleared solely via the glomeruli (filtered) and by two other substances, PAH and PSP, that are cleared chiefly if not entirely by the proximal convolutions of the nephrons (secreted).

Resorption is shown in connection with the simultaneous clearance of urea and inulin and of sodium and inulin with comment on the site and circumstances of the resorption of urea and sodium when inulin is considered as solely filtered but is not resorbed.

Maintenance of the rate of filtration during a reduction of renal blood flow as well as variations in the amount of filtration, are held to be due to differential vasomotor changes which cause efferent arterioles to be actually or relatively more constricted than the afferent. The only indication that such might occur was the observed increase in size of the glomerular tuft when minute amounts of adrenalin were added to frog's blood and a frog's kidney was perfused with it. No increase in size of this tuft was observed following a like perfusion without the addition of adrenalin.

In the human kidney the size of the lumen of all efferent arterioles except those that descend into the medulla is approximately the same as that of associated afferent arterioles. The lumen of those that descend into the medulla is several microns larger. The thickness of the wall of efferent arterioles except those that descend into the medulla is one-third less than that of associated afferent arterioles. The wall of those that descend into the medulla is as thick as or slightly thicker than the wall of associated afferent arterioles. A structural basis for the differential constriction of afferent and efferent arterioles, such as would explain maintenance of the rate or amount of filtration during a reduction of renal blood flow, is not apparent from these measurements.

The Journal of Urology
Vol 75 No 2 February 1956
Printed in U S A

THE EFFECT OF TEMPERATURE, HUMIDITY AND DEHYDRATION ON THE FORMATION OF RENAL CALCULI

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It is generally conceded that there is no one etiological factor responsible for the formation of renal calculi. Endogenous factors undoubtedly playing a part in their formation are obstruction, infection, metabolic disturbances including hyperparathyroidism, renal acidosis and hypercalcinuria Exogenous factors possibly of influence include diet, water, soil, and climatic conditions The beautiful *investigative work being carried on by Baker*[1], *Boyce*[2] *and others in this* country, and by Carr[3] in England is of fundamental importance and should add much to our knowledge of the etiology and management of renal calculi However, we believe that further investigation of the epidemiological aspects of calculus disease might also prove to be of great assistance in establishing more definitely the etiology of nephrolithiasis There have been described for years certain "stone-forming areas" scattered throughout the world where urolithiasis is particularly common Maps depicting these areas are frequently seen in the literature The original studies on which most of these maps are based, however, were made many years ago and apply chiefly to vesical calculi, and not to the incidence of renal calculi In this light, the geographical distribution of renal calculi should be restudied, because the great majority form under entirely different circumstances than do vesical calculi The incidence of vesical lithiasis has decreased, while that of nephro- and ureterolithiasis appears to be on the increase

In studies of the geographical distribution of renal calculi, the chief stone-forming areas in the United States are supposedly the Southeast, Southern California, and a longitudinal belt somewhat south of the Great Lakes Since beginning practice in Savannah 8 years ago, we have been struck by the extremely high incidence of nephro and ureterolithiasis in our vicinity In approximately 12,000 new patients seen in our office during this period, 815, or approximately 6 8 per cent, were diagnosed as having acute renal colic due to ureteral calculus There has been approximately the same incidence of nephrolithiasis The combined incidence of ureterolithiasis and nephrolithiasis approximates 14 per cent of our total office cases

Aesculapius and other profound students of human nature have stressed the influence of weather on man Hippocrates admonished us, "Whoever wishes us to pursue properly the science of medicine must proceed thus First, he ought to consider what effects each season of the year can produce, for the seasons are not

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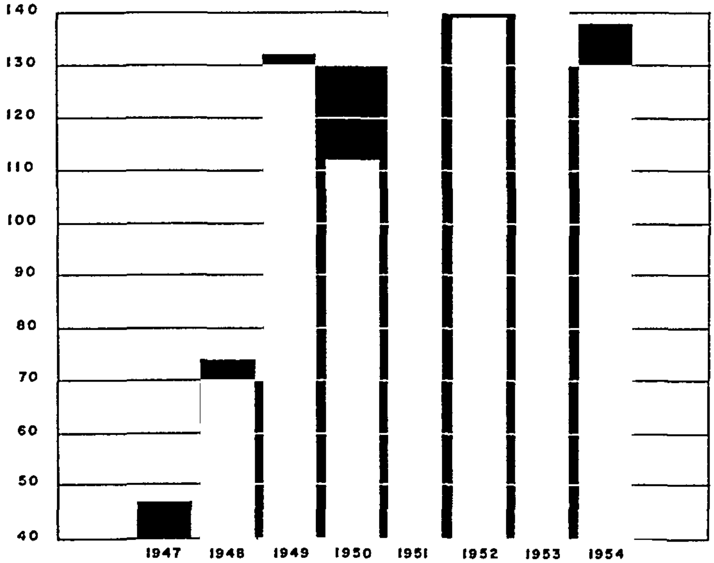
Read at annual meeting, American Urological Association, Los Angeles, Calif , May 19, 1955

[1] Baker, Roger and Sison, Francisco Demonstration of altered tissue mucopolysaccharides in renal calculus disease by *selective staining techniques* J Urol , 72 1032, 1954

[2] Boyce W H , Garvey, F K and Norfleet, C M Ion binding properties of electrophoretically homogeneous mucoproteins of urine in normal subjects and in patients with renal calculus disease J Urol , 72: 1019, 1954

[3] Carr, R J A new theory on the formation of renal calculi Brit J Urol , **26:** 105, 1954

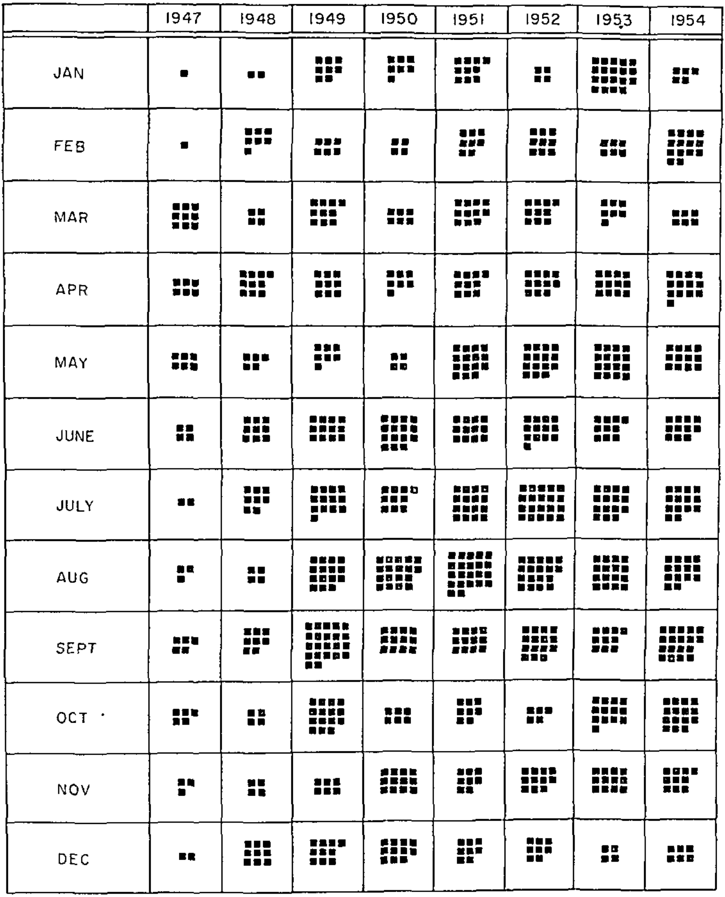


NUMBER OF ACUTE URETEROLITHIASIS SEEN PER YEAR
1947 ——— 1954

FIG. 1

alike, but differ widely both in themselves and in their changes. For with these seasons men's diseases, like their digestive organs, suffer change." During the past 8 years, we have been greatly impressed by the definite seasonal incidence of acute renal colic due to ureterolithiasis. The great majority of these cases occur in the hot months. During the period of this survey we have seen 922 such cases in 815 patients, averaging almost 135 cases a year for the past 6 years (fig. 1). The yearly incidence has remained remarkably constant throughout this latter period. For this study, we have chosen acute ureterolithiasis rather than nephrolithiasis. We believe that these small ureteral calculi give a more reliable picture as to the time of formation in the kidney than do actual renal calculi of varying sizes and causing varying symptoms. In our experience these calculi have been almost invariably composed of calcium oxalate, and/or calcium oxalate and calcium phosphate. The urinary pH in these patients is most generally slightly acid or neutral, and urinary infection is present in a surprisingly low percentage. From these studies, it seems apparent that the great majority of these calculi form with rapidity in the kidney, particularly when the weather is hottest, and rather quickly drop into the ureter and cause colic which results in their detection. We have all followed over a period of months, or even several years a small calculus in a calyceal tip, to have it finally drop into the ureter and cause renal colic. This, however, has been quite rare in this series, and very few of these calculi have been previously diagnosed. We have several instances of ureterolithiasis in which only one stone was demonstrated at the time of the initial visit, yet the patients returned within 3 to 4 weeks with a new 3 mm.–1 cm. diameter stone in the same or the opposite side, showing how rapidly these small calculi can form under favorable circumstances.

Figure 2 gives the total number of cases of acute ureterolithiasis seen each



NUMBER OF CASES OF ACUTE URETEROLITHIASIS SEEN PER MONTH
JAN 1947 TO JAN 1955

FIG. 2

month of each year over the 8-year period. From this chart it is quickly seen that the heaviest concentration of cases occurs from May through September. In this chart there are several instances in which a fairly large number of cases are seen during one of the colder months, notably January 1953, when 19 cases were seen. It should be noted in this particular instance, however, that only 8 and 6 cases were seen in the month before and the month after, respectively.

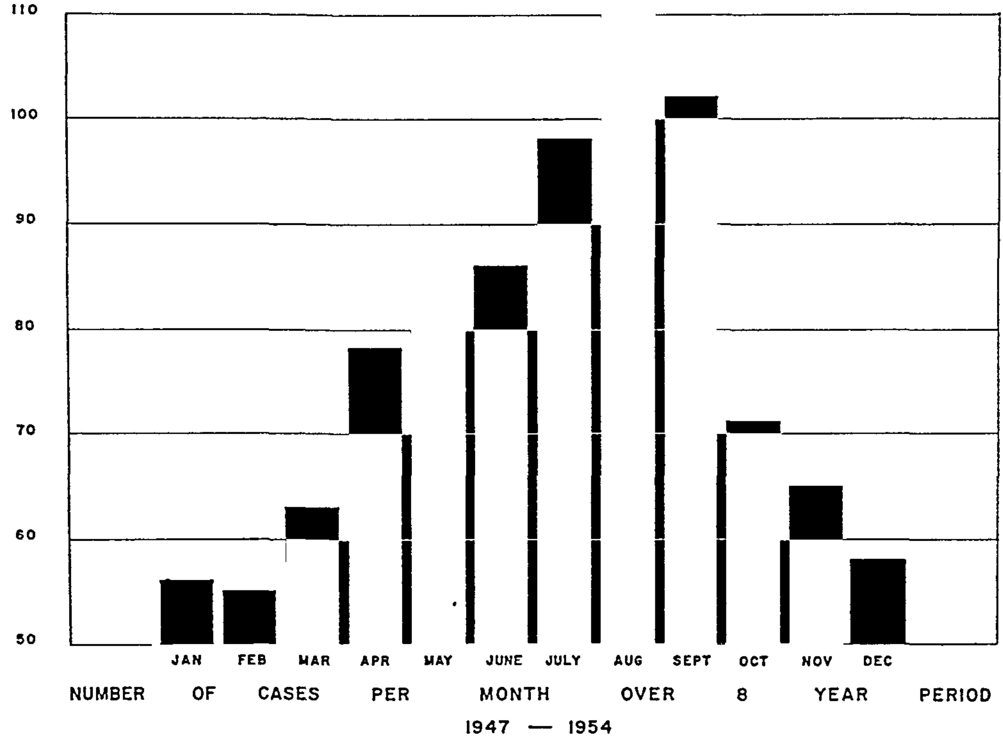


Fig. 3

Figure 3 shows graphically the total number of cases seen each month over the 8-year period. Here the marked preponderance of cases during the months April through September is even more striking, with a steady increase as the months become warmer and a steady decrease as the cold weather comes on.

Figure 4 shows the number of cases of acute ureterolithiasis seen per month for the entire 8-year period compared with the average mean temperature for the month for the same period. It will also be seen that the climate in our locality is of a temperate nature, the mean temperature varying from 52F in December to 81.2F in July. The much higher incidence of these calculi from April to October, when the average mean temperature varies from 66 to 81.2F, is most obvious. The incidence curve follows remarkably close the temperature curve throughout the year. There is a slight but definite lag phase, which may have to do with the time it takes these calculi to form and drop into the ureter. This lag phase is quite obvious when one notes the high peak of cases seen in August, which is preceded by two very hot months, June and July. The average mean temperature is almost the same in July and in August. Likewise, as the weather becomes colder, the number of cases decreases. Fewest cases have been seen in February, which follows the two coldest months of the year, December and January.

A number of authors have stated that renal calculi are relatively rare in the wet tropics, but no figures are given showing average temperature and humidity in the areas in question. Davalos[4] found renal calculi to be quite common in the

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[4] Davalos, Alfonso: The rarity of stones in the urinary tract in the wet tropics. J. Urol., 54: 182, 1945.

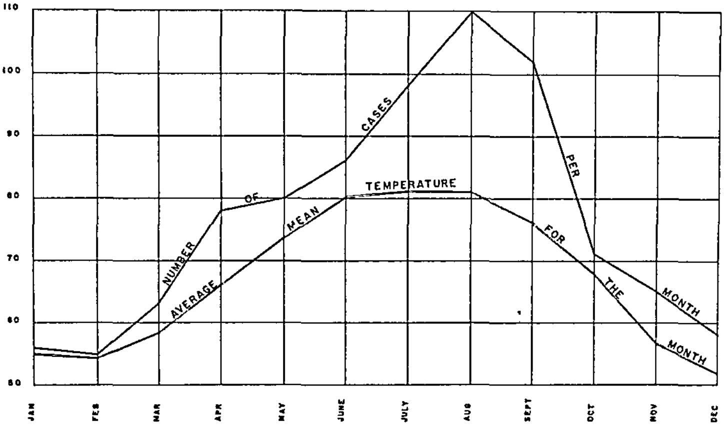

Fig 4

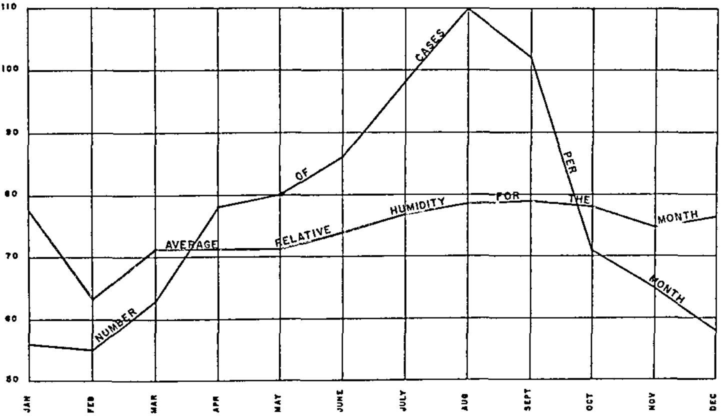

Fig 5

warm dry section of Equador, while in the warm moist section of the country they were quite rare He theorizes that excessive sweating in such climate results in the excretion of waste products by this route rather than through the kidneys, and that this is responsible for the very low incidence of renal calculi in these areas However, it would seem more logical that where the temperature is hot and the urine concentrated, there should be a definitely higher incidence of renal calculi, particularly since the usual constituents of renal calculi are not excreted to any degree by the sweat glands

Figure 5 graphically compares the number of cases of acute ureterolithiasis seen per month with average relative humidity over the 8-year period. There is little if any obvious correlation. It would seem from these figures that relative humidity has no effect on the incidence of renal calculi, unless there is some correlation between the overall rather high relative humidity and the high incidence of renal calculi in this vicinity, not shown by these studies. Perhaps further studies comparing stone incidence with relative humidity in other localities would prove to be of assistance.

Since there are only minor variations in the other possible etiological factors responsible for the formation of renal calculi from season to season, aside from temperature, one must assume from these studies that the latter plays a large and important role in their formation. Actually we do not consider temperature itself responsible, but consider the dehydration and associated urinary concentration resulting directly from the very high mean temperature seen during the hot months to be the cause. Since no other apparent factor enters in, it would seem that dehydration alone results in the very close correlation between temperature and stone incidence. We therefore feel that dehydration plays a much more important role in the formation of renal calculi than is generally realized. Butt[5] has stated in one of his papers that May to August are the "stone-forming" months in western Florida. Burkland[6] has mentioned that there is a seasonal variation in the incidence of stones seen in hot weather. Butt[5] states that dehydration, along with numerous other factors, results in a colloid-crystalloid imbalance, which may be responsible for the formation of renal calculi. The concentration of urine relatively increases the proportion of electrolytes and decreases the proportion of colloids, thereby increasing their possibility of precipitating. According to him, exposure of the body to dry heat is often a deciding factor as to whether stones will form in persons who are predisposed to calculus formation.

Another fact which suggests to us the extreme importance of dehydration in the formation of these calculi is the rarity of recurrence in this series. There have been only 79 cases of known recurrence in this entire group, an incidence of 8.8 per cent. Also, it is of interest that only 147 patients in this series gave a definite history of stone passage or removal previously. It would seem that the invariable admonition to the patient to "force fluids" after stone passage or removal has had its effect.

SUMMARY AND CONCLUSIONS

The epidemiological aspects of renal calculi are of great scientific interest, and further investigation along these lines might be of assistance in establishing more definitely their etiology.

A series of 922 consecutive cases of acute renal colic due to ureterolithiasis is presented. In this series a definite and striking seasonal incidence of the disease has been shown to exist.

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The incidence of acute ureterolithiasis follows to a remarkable degree the average mean temperature; the greatest number of cases were seen from April to October, and the fewest in February. We are of the opinion that the high average mean temperature existing from April to October results in dehydration and urinary concentration with resultant increased stone formation during these months.

Dehydration plays a much more important role in the formation of renal calculi than is generally realized. We believe that if patients can be made to take large quantities of liquid, particularly in the hot months, the number of cases of acute ureterolithiasis can be very significantly reduced.

In this series, relative humidity has apparently had no definite influence on the incidence of acute ureterolithiasis.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

THE INFLUENCE OF THE DIET ON URINARY CITRATE EXCRETION

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The mechanism of urinary calculus formation is undoubtedly a complicated one in which many factors may be involved. Such factors as an elevated calcium excretion and increased pH of the urine are widely accepted. Among other factors deserving consideration is the presence of organic substances in urine capable of complexing calcium ions and thus holding them in solution. The occurrence of comparatively large amounts of citrate in urine was earlier pointed out by Amberg and McClure.[1] The urinary citrate, expressed as mg. anhydrous citric acid per day, has been shown to vary between the limits of 0.1 to 1.5 gm. per day.[2] Kissen and Locks[2] and Scott and co-workers[3] have indicated that citrate excretion in patients forming urinary calculi is considerably depressed as compared to normal individuals. Shorr, et al.[4] have reported a decreased citrate excretion in cases of two chronic stone formers during a stone-free interval. On the other hand Conway, Maitland and Rennie[5] have attributed the decreased citrate excretion in calculus patients to the presence of infecting bacteria capable of splitting citric acid. Urinary calculi consisting mainly of calcium citrate have been experimentally produced in the rat by Morris and Steenbock.[6] The animals were placed on a low phosphate, normal calcium diet and the calcium citrate calculi so produced could be converted to the carbonate-phosphate type of stone by increasing the amount of alkali in the diet. In addition Lawrie[7] has recently reported an apparent response of a case of nephrocalcinosis to citrate therapy.

In view of the findings of the various workers reported above, information concerning the factors involved in the urinary excretion of citric acid should be

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Accepted for publication June 29, 1955.

This investigation was supported by a research grant (PHS A-248) from the National Institute of Arthritis and Metabolic Diseases of the National Institutes of Health, Public Health Service.

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[5] Conway, N. S., Maitland, A. I. L. and Rennie, J. B.: The urinary citrate excretion in patients with renal calculi. Brit. J. Urol., 21: 30–38, 1949.

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[7] Lawrie, T. D.: Nephrocalcinosis: a report of a case showing an apparent response to citrate therapy. Glascow Med. J., 35: 128–133, 1954.

of considerable significance Several workers[8–12] have shown that the excretion of citrate varies with the pH of urine, the ingestion of alkali increases the urinary citrate excretion whereas the ingestion of acid decreases it Hormonal influences, particularly parathormone[13, 14] and estrogens[15] have also been shown to influence citrate excretion Perhaps the increase in citrate excretion in women with increase in estrogen production during the menstrual cycle may be a factor in the lower incidence of urinary calculi in women as compared to men

Vitamin D administration in physiological as well as in massive doses has been shown to increase the blood, bone, kidney and urine levels[16, 17, 18] Although vitamin D administration has been demonstrated to increase urinary pH, Steenbock and co-workers[19] have produced evidence to indicate that its action upon citrate excretion is at least partially independent of the change in urinary pH, since they were able to show an increased citrate excretion in rats on an acid or alkaline diet whenever vitamin D was incorporated in the diet

In the case of the increase in citrate excretion accompanying alkalinization of the urine, a specific mechanism involved with acid-base balance has been postulated by Ostberg,[20] and does not involve mobilization of body stores such as that found in bone[21, 22]

Smith and Meyer[23] investigated the influence of diet on the urinary excretion

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[8] Kuyper, A C and Mattill, H A Some aspects of citric acid metabolism J Biol Chem 103 51–60, 1933

[9] Schuck C Urinary excretion of citric acid II Effect of ingestion of citric acid, sodium citrate and sodium bicarbonate J Nutrition, 7 691–700, 1934

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[22] Class R N and Smith, A H The skeleton as a source of endogenous citric acid J Biol Chem 151: 363–368, 1943

[23] Smith A H and Meyer C E The influence of diet on the endogenous production of citric acid J Biol Chem 131 45 55 1939

of citrate and reported that maximal excretion of citrate was obtained on a high carbohydrate diet, followed by a high fat diet as the next most productive, while a high protein diet was found to be the least productive of urinary citrate. On the other hand, Kuyper and Mattill[8] found an increase in citrate excretion in humans following a meal consisting of eggs and toast. This discrepancy may be partially explainable on the basis of the vitamin D content of eggs. Schuck[24] has reported an increased citrate excretion in women following the ingestion of grape or orange juice. This increased citrate excretion was probably related to the alkali effect of the juices since an increase in urinary pH was also noted.

The level of citrate in the urine of a given subject at any one time appears to be the result of the balance of a number of factors such as acid or alkali in the diet, vitamin D and hormonal influences. The quantitative aspect of such a balance has not as yet been worked out.

In consideration of the well-known calcium complexing abilities of citrate plus the implications from the literature that citrate plays some role in urinary calculus formation, further information on the influence of diet on the urinary excretion of citrate would seem to be desirable.

EXPERIMENTAL

The 24-hour urinary citrate excretion was followed on 54 medical students on their normal self-selected diets. These students were then divided up into groups of varying sizes, and their citrate excretion was determined, while on an assigned diet.

Composition of the diets. High protein diet: A diet made up primarily of meats, cheese, eggs, milk and other dairy products at each meal, plus a high protein snack before retiring at night.

Low protein diet: Essentially a high carbohydrate diet in which meat. eggs, cheese, milk, and leguminous vegetables were excluded. Intake of bread was held to a minimum.

Potato diet: A diet similar to the low protein diet but consisting almost entirely of potatoes and other root vegetables.

Fasting diet: First day—normal diet; second and third days—complete fast. Subject was allowed to have water *ad lib.*

Acid diets: a. Ammonium chloride: First day—normal diet; second day—normal diet plus 1 gm. ammonium chloride at each meal; third day—normal diet plus 1 gm. of ammonium chloride at each meal, mid-morning, mid-afternoon, and at bedtime.

b. Prunes: First day—normal diet; second day—normal diet plus 2 dozen prunes; third day—normal diet plus at least four dozen prunes spread throughout the day. The acid quality of this diet depends upon the presence in prunes of organic acids not metabolized in the body.

Alkaline diets: a. Citrus fruits: First day—normal diet; second day—normal diet plus six oranges at night; third day—normal diet plus two to three dozen oranges distributed throughout the day.

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b Sodium citrate: First and second days—normal diet, third day—normal diet plus 10 gm of sodium citrate before each meal

c Sodium bicarbonate. First and second days—normal diet, third day—normal diet plus 10 gm of sodium bicarbonate before each meal

In each case where the normal diet supplemented with the various constituents above was used, the subjects were required to maintain a diet conforming as closely as possible to that consumed during the time of the collection of the normal twenty-four hour urine All diets covered a three-day period unless otherwise noted On the last (third) day of the dietary period twenty four-hour urine collections were made and preserved over chloroform No attempt was made to prevent loss of carbon dioxide from the urine, and for this reason the pH values for the urines in the pH 8 range may be somewhat in error

Determination of the urinary pH was made with the Beckman model G pH meter, using the glass electrode

Citrates were determined by the method of Ettinger and co-workers[25] This procedures relies essentially upon the oxidation of citric acid to pentabromo acetone in the presence of permanganate and bromine The pentabromoacetone when allowed to react with alkaline pyridine produces a pink color which may be measured phometrically

RESULTS

The results of the determination of citrate excretion by humans on various dietary regimes are shown in tables 1, 2, 3 and 4 In each of the tables, the first column identifies the subject, the second lists the particular diet used, the third column indicates pH of the urines, and the fourth shows citrate excretion in terms of milligrams of anhydrous citric acid per day

Table 1 shows the data obtained upon the high and low protein, potato and fasting diets In the case of the high protein diet, although in most cases the pH of the urines decreased as expected, the citrate excretion in six of the 8 cases increased and in the other two it remained relatively unchanged No definite trend could be established from the data on the low protein diet The potato diet in the 4 cases studied produced increases in both urinary pH and citrate excretion The fasting experiments showed no essential change in one case, a slight decrease in a second, and in the third case a decrease was noted on the first day of the fast, with an enormous increase appearing on the second day of the fasting period This latter increase may have been caused by an increased ketone body excretion

The results obtained on the acid diets, table 2, show that although decreases in the urinary pH were obtained on the ammonium chloride diet, there was a decrease in citrate excretion in only two out of the 6 cases studied In the other 4 cases the excretion of citrate actually increased In the case of the prune diet three of 5 cases showed a positive correlation between change in urinary pH and citrate excretion In the other two, the citrate excretion increased although

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[25] Ettinger R H , Goldbaum, L R and Smith, H L A simplified method for the determination of citric acid in biological fluids J Biol Chem , 199. 531 536, 1952

TABLE 1. *Citrate excretion by humans on high protein, low protein, potato or fasting diets*

Subject	Diet	Urine pH	Urinary Citrate mg./24 hr.	Subject	Diet	Urine pH	Urinary Citrate mg./24 hr.	Subject	Diet	Urine pH	Urinary Citrate mg./24 hr.
JLB	Normal	6.38	736	WRS	Normal	6.00	846	PC	Normal	6.60	806
	High protein	5.62	1034		Low protein	6.20	920		Potato	6.80	1000
WNL	Normal	6.20	666	CCH	Normal	6.33	1751	AJC	Normal	5.62	797
	High protein	6.00	920		Low protein	6.30	1060		Potato	6.20	833
CF	Normal	6.02	634	TH	Normal	6.70	694	JJP	Normal	5.70	447
	High protein	5.42	810		Low protein	6.50	551		Potato	6.28	925
PMW	Normal	6.20	855	GWH	Normal	6.30	592	JRH	Normal	5.16	1080
	High protein	6.00	1370		Low protein	6.10	512		Potato	6.10	1037
CS	Normal	6.30	394	DCB	Normal	6.50	694	JSH	Normal	6.20	568
	High protein	6.30	900		Low protein	6.70	570		Fasting 1 day	6.15	328
LRB	Normal	6.20	776	CLB	Normal	6.15	372		Fasting 2 day	6.05	4070
	High protein	6.45	1093		Low protein	6.95	654	JLW	Normal	6.37	476
FRS	Normal	5.90	850	CWP	Normal	6.00	1054		Fasting 1 day	6.30	554
	High protein	5.87	845		Low protein	6.10	570		Fasting 2 day	5.75	488
VM	Normal	6.20	626	AWH	Normal	5.90	620	JWT	Normal	6.72	539
	High protein	6.50	643		Low protein	6.70	401		Fasting 1 day	5.45	220
									Fasting 2 day	5.40	359

TABLE 2. *Citrate excretion by humans on acid diets*

Subject	Diet	Urine pH	Urinary Citrate mg./24 hr.	Subject	Diet	Urine pH	Urinary Citrate mg./24 hr.
AGM	Normal	6.71	432	ARK	Normal	6.45	644
	Ammonium chloride	6.34	1260		Prunes	5.80	558
EGA	Normal	6.50	610	MDF	Normal	6.70	720
	Ammonium chloride	6.45	798		Prunes	6.10	560
JRE	Normal	6.59	209	TC	Normal	5.80	568
	Ammonium chloride	6.25	1036		Prunes	6.00	700
RF	Normal	6.49	400	WCE	Normal	6.07	487
	Ammonium chloride	5.95	1486		Prunes	5.65	594
JWS	Normal	6.76	589	DC	Normal	6.20	484
	Ammonium chloride	6.05	516		Prunes	5.72	700
J de B	Normal	6.60	1048				
	Ammonium chloride	6.00	480				

the pH of the urine decreased. Since these subjects were allowed to consume their normal diet supplemented with ammonium chloride or with prunes, the discrepancy between these findings and those reported by other workers could be caused by variation in the vitamin D intake. For this reason another group of six students was placed on the ammonium chloride diet with the further restriction that they avoid all dairy products, the usual dietary source of vitamin D. These results, table 3, are in agreement with the well-known effect of acid ingestion on citrate excretion. In each case a decrease in urinary pH was accompanied by a decrease in citrate excretion.

The results on the alkaline diets, table 4, are more in keeping with the evidence in the literature that citrate excretion is increased upon alkalinizing the

TABLE 3 *Citrate excretion by humans on a diet free of dairy products, but supplemented with ammonium chloride*

Subject	Diet	Urine pH	Urinary Citrate mg /24 hr	Subject	Diet	Urine pH	Urinary Citrate mg /24 hr
DEJ	Normal	6 10	677	CCH	Normal	6 33	1751
	Ammonium chloride	6 10	448		Ammonium chloride	5 70	1167
AWG	Normal	6 02	460	WRS	Normal	6 00	846
	Ammonium chloride	5 25	420		Ammonium chloride	5 30	420
BET	Normal	5 60	706	JS	Normal	6 76	589
	Ammonium chloride	5 50	530		Ammonium chloride	5 95	294

TABLE 4 *Citrate excretion by humans on various alkaline diets*

Subject	Diet	Urine pH	Urinary Citrate mg / 24 hr	Subject	Diet	Urine pH	Urinary Citrate mg / 24 hr	Subject	Diet	Urine pH	Urinary Citrate mg / 24 hr
WRB	Normal	5 95	422	GEE	Normal	5 65	379	JDB	Normal	5 90	604
	Citrus fruit	6 45	896		Sodium citrate	7 59	900		Sodium bicarbonate	7 20	1452
AWG	Normal	6 02	460	MLC	Normal	6 00	859	CC*	Normal	5 60	646
	Citrus fruit	5 70	482		Sodium citrate	7 26	1019		Sodium bicarbonate	8 25	1629
MMW	Normal	6 22	890	PDM	Normal	5 97	900	RFH	Normal	5 99	378
	Citrus fruit	7 27	1570		Sodium citrate	7 5[illegible]	869		Sodium bicarbonate	8 01	825
PM	Normal	6 12	486	RAF	Normal	5 80	644	BET	Normal	5 60	706
	Citrus fruit	7 21	1206		Sodium citrate	8 15	878		Sodium bicarbonate	7 70	818
TLO	Normal	6 25	771	WRB	Normal	6 04	746	HEA	Normal	5 87	1268
	Citrus fruit	6 40	868		Sodium citrate	7 86	1129		Sodium bicarbonate	7 60	756
DEJ	Normal	6 10	677	GB*	Normal	6 20	1163	GFK	Normal	5 60	1435
	Citrus fruit	6 80	1701		Sodium citrate	8 45	1035		Sodium bicarbonate	7 92	775
RH*	Normal	6 20	555	JAM	Normal	5 85	481	JE	Normal	5 98	684
	Citrus fruit	6 30	599		Sodium citrate	8 07	1330		Sodium bicarbonate	7 80	525

* Females

diet Good agreement was obtained on the citrus fruit diet, increase in urinary pH, where obtained, in each case produced an increased citrate excretion On both the sodium bicarbonate and sodium citrate diets a few cases were noted where an increase in urinary pH did not produce an increased citrate excretion In all but one of these cases the citrate excretion on the normal diet was quite high, and again variation of vitamin D intake could have been a factor Also these diets usually produced a mild diarrhea (severe in one case) It is conceivable that the diarrhea could have had some effect on the results obtained in these experiments

All of the results on the dietary study must of necessity suffer from the criticism that the dietary regimens were not subject to rigid control This may account for some of the variation noted

DISCUSSION

From the data just presented, it is evident that in the human, the acid or alkali content of the diet is not the only factor concerned in citrate excretion The production of increases in citrate excretion on acid containing diets such as the high protein and ammonium chloride diets is believed to be related to the vitamin D content of the diet, since in the case of the ammonium chloride diet, exclusion of eggs and dairy products, the usual dietary sources of vitamin D, brought about a decrease in citrate excretion with acidification of the urine. The presence of vitamin D in the diets used probably accounts for the fact that an elevated citrate excretion occurred on the high protein diet.

The finding of an elevated citrate excretion on the alkaline diets confirms the many earlier reports in the literature.

In relation to the problem of the calcium type urolithiasis, the selection of a high protein diet containing physiological amounts of vitamin D would appear to be quite satisfactory in two ways. First, high protein diets are usually acid-producing diets because of their sulfur and phosphorus content and therefore tend to keep the pH of the urine low (about 6.0). Second, inclusion of physiological amounts of vitamin D in the diet would tend to keep the citrate excretion high, thus supplying a complexing agent for keeping calcium in solution in the urine. Excessive intake of vitamin D should be avoided since it would cause an increased absorption of calcium from the intestine as well as increasing urinary pH and calcium excretion.

Acid-producing diets favor an increased absorption of calcium from the intestine with a resultant increase in the urine calcium level. The selection of a diet for calculus patients will require a careful balance of the factors tending to decrease urinary pH and increase urine citrate levels against those factors tending to increase both urine pH and urinary calcium excretion. The optimal conditions as regards urine pH and citrate concentration for keeping calcium in solution or for dissolution of calcium type calculi are at present unknown.

The other diets producing an increased citrate excretion would be less satisfactory since they also tend to alkalinize the urine. This increased alkalinity would tend to cause calcium to precipitate from the urine, even in the presence of increased amounts of citrate, or could possibly cause formation of calcium citrate calculi.

SUMMARY

Citrate excretion has been studied in the human under several dietary regimens.

Citrate excretion in the human is increased by the ingestion of alkali and decreased by the ingestion of acid.

The vitamin D content of the diet also affects the citrate excretion. The presence of physiological amounts of vitamin D in the diet appears to increase citrate excretion even on acid-producing diets such as high protein diets, or diets supplemented with ammonium chloride.

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

TRUE PROLAPSE OF THE URETER: CASE REPORT AND REVIEW OF THE LITERATURE

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One of the rarest anomalies of the ureter is true prolapse or herniation. The aim of this paper is to discuss the lesion, its possible etiology, clarify criteria for its diagnosis and review the literature on the subject. A case of massive true prolapse of the ureter associated with contracted bladder neck and contralateral stenosis of the ureteral meatus will be reported.

CASE REPORT

A 2½-year-old white boy entered the Department of Urology of Queens General Hospital on October 14, 1953. The mother gave a 1-year history of hourly urination with a weak stream, marked straining and pain on urination and almost constant dribbling of urine. The history was otherwise unremarkable.

The child was well developed and well nourished, in apparent good health. Four residual urine determinations ranged from 22 to 30 cc. Fasting blood sugar, blood urea nitrogen, blood count and urinalysis were within normal limits. Urine culture was sterile. Excretory urography revealed prompt function bilaterally in 5 minutes; bilateral hydroureteronephrosis was present, moderate on the left, minimal on the right (fig. 1, *A*). Cystogram revealed no reflux, either immediate or delayed. Of interest was a flat bladder base, with complete absence of funnelling, suggesting a diagnosis of contracted bladder neck (fig. 1, *B*). Panendoscopy revealed a severe iris type contracture of the bladder neck, with a pinpoint internal urethral orifice. Deep cellules and trabeculations of the bladder were present. A large tubular mass, occasionally contracting, was noted intravesically lying against the bladder neck. Its size, and the location of its base, were not determined with certainty, but it was believed to be a left ureterocele. Its orifice could not be visualized because the terminal end of this structure lay well across the midline on the opposite side of the bladder. The right ureteral orifice was in the normal position and pinpoint in size. A diagnosis of bladder neck contracture and left ureterocele was made. On October 27, 1953, under open drop ether anesthesia, the bladder was opened suprapubically. Inspection revealed a collapsed tubular structure 4 cm. long. It had the diameter of a lead pencil with its proximal end attached to the trigone on the left ureteric bar. The distal end lay free in the bladder. Its mouth was patulous, admitting the end of a large Kelly clamp with ease. A 12F soft rubber catheter was readily passed through the meatus of this structure up to the left kidney. This structure was amputated at its base. With a few interrupted catgut sutures the mucosa of the bladder was sutured to the ureteral mucosa. This resulted in a dilated ureteral orifice that

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Read at annual residents' meeting of the Brooklyn Urological Society, April 13, 1954.
Accepted for publication July 7, 1954. Publication delayed because author entered the Armed Forces and galley proof did not reach him. *Editor*

was flush with the bladder floor. The right ureteral orifice was then identified and found to be impervious to a 3F ureteral catheter. Meatotomy with the cutting electrode was performed, resulting in easy passage of a 5F ureteral catheter to the kidney. Excellent exposure of the bladder neck was then obtained by extending the original bladder incision 3 to 4 mm. distal to the bladder neck, onto the prostatic capsule. From this retropubic position an Allis clamp was placed on the neck at 6 o'clock and a broad wedge of tissue extending from 4 to 8 o'clock was easily resected with the cutting electrode. The incision of the prostatic capsule and the lower portion of the bladder was then closed. The tip of the index finger was then easily passed into the prostatic urethra from the bladder. The bladder

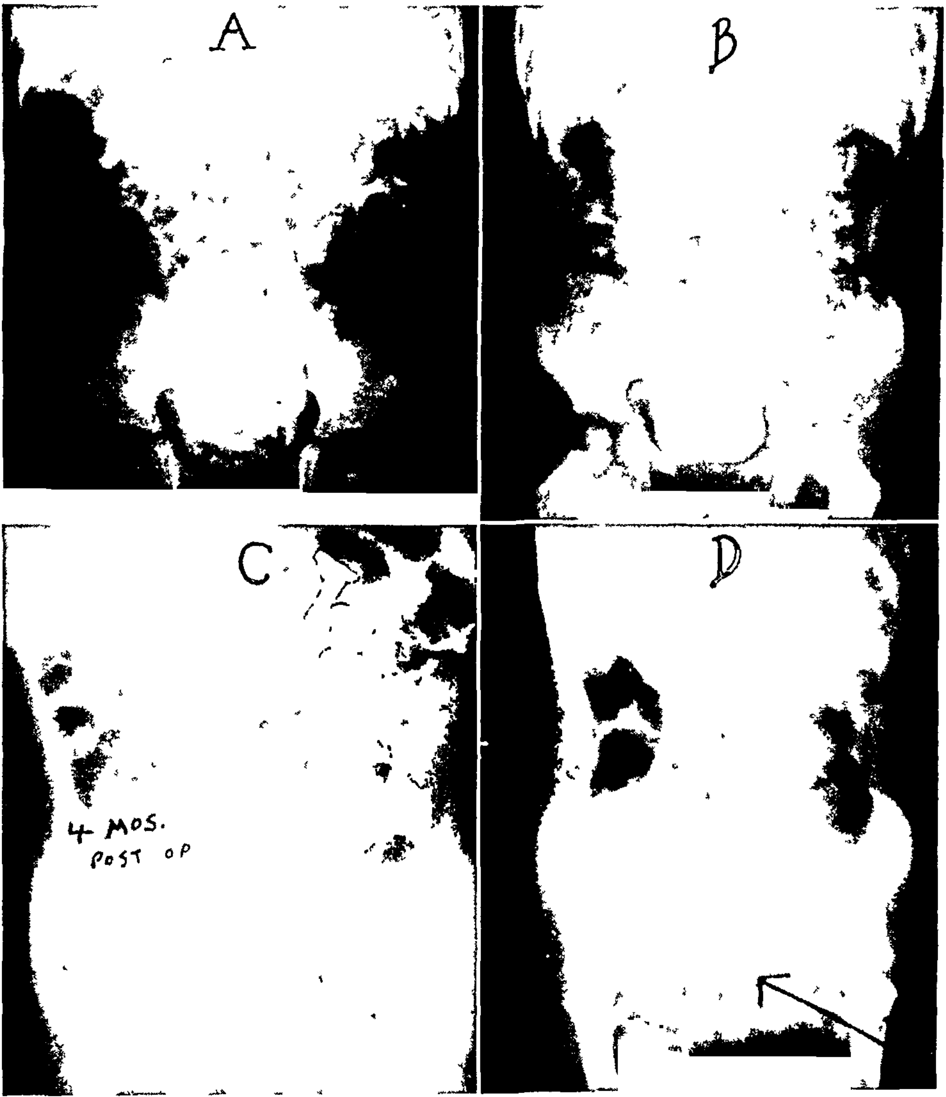

FIG. 1 *A*, preoperative excretory urogram (20 minute film) shows bilateral hydronephrosis. *B*, preoperative cystogram shows flat bladder base strongly suggestive of contracted bladder neck. *C*, 4 months postoperative excretory urogram (20 minute film) shows normal right upper tract and moderate diminution of left hydronephrosis. *D*, 2 months postoperative excretory cystogram shows excellent funnelling of bladder neck.

was closed about a 28F dePezzer tube, and transfixed to the rectus sheath. The abdominal wall was closed in layers with drainage.

Pathological report (Dr. Alfred August). The gross specimen measured 4 cm. in length by 0.6 cm. in diameter. Its walls were 0.1 cm. to 0.15 cm. in thickness and appeared to be covered with mucosa on all surfaces. The distal uncut end was patulous, the meatus being 0.5 cm. in diameter. Microscopically the structure was seen to be covered externally with ureteral mucosa. It was also lined with ureteral mucosa that was thrown into convolutions. Between these two layers of ureteral mucosa were several layers of smooth muscle. Diagnosis: Prolapsed ureter.

The postoperative course was complicated by severe urosepsis which responded slowly to antibiotics and precluded urethral catheter drainage. The suprapubic sinus closed by the fourth week. By then the child was voiding with an excellent stream and without pain. Residual urine determinations varied from 0 to 7 cc. He has been followed in the clinic for the past 6 months during which time there has been complete freedom from fever or pain. Voiding is normal with zero to 5 cc. residuals. A 16F soft rubber catheter passed with ease through the urethra to the bladder. X-ray studies were made 4 months postoperatively. Excretory urography showed moderate diminution of the left hydronephrosis. The right upper tract now appeared normal (fig. 1, *C*). A cystogram showed immediate bilateral vesicoureteral reflux (which was absent 2 months later, i.e., 6 months postoperatively). Also noted was excellent funnelling of the bladder neck which was absent in the preoperative films because of contracture (fig. 1, *D*).

DISCUSSION

An exhaustive review of the English medical literature, from the first edition of the Cumulative Index in 1916 to the present, fails to reveal a single positive case of prolapse of the ureter. A cursory review of the French literature since that time has uncovered 2 cases, both of which were not proven by surgical biopsy and cannot be diagnosed as ureteral prolapse with certainty. These cases will be discussed.

Few of the modern urological textbooks mention and describe this lesion. Ureteral prolapse is described by Hinman[1] and by Campbell[2] in their books, but no definite case reports are cited.

The literature is replete with case reports entitled, "Prolapse of the Ureter," which, on perusal, reveal that the lesion being described is in reality a ureterocele, i.e., a ballooning out of the ureterovesical mucosa due to obstruction secondary to stricture of the ureteral meatus. A ureterocele is covered on its vesical side by bladder mucosa, its lumen is lined with ureteral mucosa and its walls contain no muscle. Ureteral prolapse may be defined as that condition in which there is herniation through the ureteral meatus of the mucosal and muscular coats of the ureter into the bladder. It is characterized by the presence of ureteral mucosa covering the vesical side of the prolapse and of course, lining its lumen with

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[1] Hinman, F.: The Principles and Practice of Urology. Philadelphia: W. B. Saunders Co., 1936.

[2] Campbell, M.: Clinical Pediatric Urology. Philadelphia: W. B. Saunders Co., 1951.

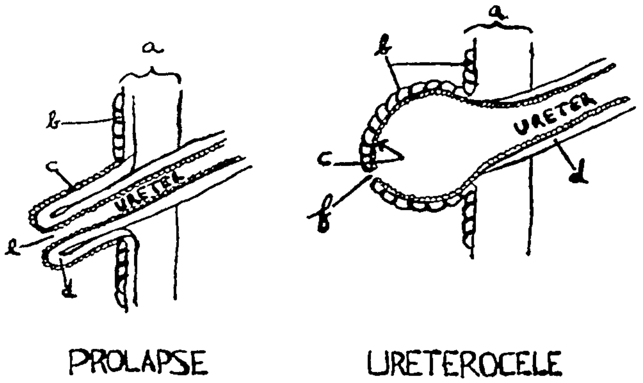

Fig. 2. Diagrammatic comparison of prolapse of ureter and ureterocele. *a*, Bladder wall. *b*, Bladder mucosa. *c*, Ureteral mucosa. *d*, Ureteral musculature. *e*, Normal or dilated ureteral orifice. *f*, Stenotic ureteral orifice.

ureteral musculature contained between these mucosal layers (fig. 2). A possible exception to this definition is the case reported by Filho[3] (to be discussed) in which he described prolapse of only the ureteral mucosa. Unfortunately this was not proven by biopsy.

The ureteral meatus in prolapse of the ureter may be normal or enlarged in size, or possibly stenotic (this latter condition described in Filho's case to be discussed below). Hinman[1] states that "the orifice may be large . . . but even in this instance there is some obstruction and urinary flow may give ballooning and cystic formation." In the case herein reported the meatus was large, being 5 mm. in diameter, yet cystoscopically the prolapse had the appearance of a ureterocele and the entire upper tract was markedly dilated. In view of the presence of a severe contracture of the bladder neck, the part played in the pathogenesis of the hydroureter and hydronephrosis by the ureteral prolapse *per se* cannot be determined in this case.

Papin, cited by Filho,[3] thought that the mechanism of prolapse required a dilated ureteral meatus. In Uteau's[4] case the right orifices were double and normal in appearance. In the region of the left orifice "a quadrilateral fleshy outpocketing" was noted, at the summit of which a ureteral orifice was seen. He stated that on making pressure on the summit with his bougie the outpocketing inverted, completely disappearing and allowing the bougie to pass easily to the kidney. On removal of the bougie the region of the orifice appeared normal, and the lesion which he termed ureteral prolapse remained completely reduced. Unfortunately Uteau makes no mention of the condition of the upper ureter and kidney, of the caliber of the ureteral meatus, of the size of the lesion or of a followup cystoscopy. From his description this lesion may have been a ureterocele that was temporarily inverted by the bougie.

Filho[3] felt that stricture of the ureteral meatus was necessary for the formation of prolapse. His case was that of a young woman with intermittent bouts of renal colic and hematuria. On cystoscopy he first thought he saw bilateral trigonal papillomas appearing and disappearing. Further observation revealed that during ureteral systole the bladder wall surrounding the ureteral meatus was raised, taking the form of a sphere. The meatus was very small and resistant, having a border resembling a fibrous cord which, after much manipulation and dilatation, admitted a 5F catheter. During the period of diastole everything changed. The bladder wall flattened out and it appeared that the ureteral mucosa which lined the inferior extremity of the ureter escaped through the meatus and presented itself in the bladder cavity, resembling a polyp. With each new ejaculation of urine the prolapsed tissue re-introduced itself through the meatus into the ureteral lumen and the outpocketing surrounding the meatus again formed. The tissue was seen to bleed lightly on prolapsing through the meatus. Even after passing a catheter through the meatus to the kidney, this prolapse returned in ureteral diastole. The aforementioned process was seen to occur bilaterally. Unfortunately this tissue was not biopsied nor was its size reported. No mention was made of the condition of the upper tracts and followup studies were not possible because the patient was lost to view. An unusual aspect of this case is that the prolapsing tissue (which from Filho's description was either ureteral mucosa or papilloma) passed through a small or stenotic meatus and did so during diastole.

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[3] Filho: J' d'urol., **34:** 133, 1932.

[4] Uteau: J' d'urol., **18:** 473, 1924.

In MacGowan and Maner's[5] case the ureters descending from the kidneys in their normal course pierced the bladder in their normal positions and became continuous with one another in the form of a loop across the trigone. At necropsy, the index finger could easily be passed beneath this loop. There was a meatus on the right side laterally placed as the ureter emerged from the bladder wall. On the left side the meatus was on the anterolateral aspect of the ureteral loop and 1 cm. distal to the site where the ureter emerged from the bladder wall. There was complete patency of the left ureter continuing through the loop to a point one centimeter beyond and to the right of the anomalous left ureteral orifice. Beyond this point it was occluded by a tuberculous inflammatory process which extended up the right ureter for several centimeters. Both kidneys were involved with tuberculous infections. It is difficult to state whether this rare anomaly of intravesical fusion of the terminal ends of the ureters represents in part ureteral prolapse. I can only postulate that the cause of this anomaly might be that the ureteral buds in addition to growing in the normal extravesical direction also grew intravesically, met and fused.

The etiology of prolapse in the case herein reported cannot be explained with certainty. As was postulated to have occurred bilaterally in MacGowan and Maner's case, unilateral intravesical growth of the ureteral bud may have caused this anomaly. Excluding the ureteral bud theory one might postulate that a deficiency of the periureteral sheath was present, resulting in poor ureteral fixation and support. This condition, coupled with a normal or dilated ureteral meatus, may have led to prolapse.

It is difficult to conceive of this anomaly occurring in the absence of a normal or a dilated ureteral meatus.

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[5] MacGowan, Granville and Maner, G. D.: J. Urol., **11:** 199, 1924.

CONCLUSIONS

Prolapse of the ureter is a rare anomaly. It is necessary to differentiate between it and ureterocele. A prolapse is covered on both sides with ureteral mucosa, between the layers of which is found ureteral musculature. The meatus is normal or dilated in size. Ureterocele is covered on its bladder side by the vesical mucosa, its lumen is lined with ureteral mucosa, and its walls contain no musculature. Its orifice is stenotic.

The etiology of ureteral prolapse is unknown. It is postulated that its formation may occur in utero due to intravesical growth of the ureteral bud. Another causative factor may be a deficiency of the periureteral sheath resulting in poor ureteral fixation.

SUMMARY

A case of massive true prolapse of the ureter is reported in association with contralateral ureteral meatal stenosis and contracture of the bladder neck in a 2½-year-old boy. The literature is reviewed on the subject and a clarification of the criteria for its diagnosis is made. Possible etiologic factors are postulated.

This is apparently the first case of true ureteral prolapse proven by pathological study to be reported in the modern literature.

168 Bon Air Ave., New Rochelle, N. Y.

The Journal of Urology
Vol 75 No 2 February 1956
Printed in U S A

A METHOD FOR RELIEF OF UPPER URETERAL OBSTRUCTION WITHIN BIFURCATION OF RENAL ARTERY

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The following procedure, for alleviating upper ureteral obstruction implicated by a lower polar renal artery, is being presented because It is simple, it directly remedies what appears to be the initiating anatomical defect, it has been maximally effective in two consecutive cases, it is conservative of renal parenchyma, diligent literary search and inquiry of colleagues have not located it elsewhere, and we believe it warrants early trial by others

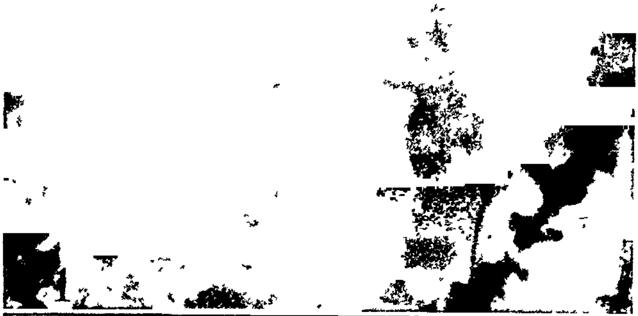
Winsbury-White ('25) advanced the concept that when hydronephrosis is secondary to an obstructing vessel it is usually acquired during postnatal growth The presumption is that such hydronephrosis is due to herniation of renal pelvis, typically between an extrahilar bifurcation of the renal artery Herniation would occur through the surface of least resistance, that is, anteriorly Evidence for this exists in the Discussion Our method has been to mobilize pelvis and upper ureter and to seal off the anatomical or hernial defect between the two branches of the bifurcating vessel

MATERIAL AND METHOD

Two consecutive cases with hydronephrosis implicated by a lower polar renal artery were operated upon by the method put forward

Case 1 (VAH 43395), a 25-year-old Caucasian man was admitted with chief complaint of nausea and sudden severe pain in the right renal region radiating to the right lower quadrant This pain first appeared when he was 23 and recurred often He had no history of dysuria, pollakiuria, hematuria, chills, or fever He drank moderately of beer or whiskey on occasion He had had several bouts of diarrhea since the age of 23 He was slender, well developed, and well nourished At time of examination his pain had subsided and he was not ill, his oral temperature was 98 6F, pulse 88 per minute, and arterial pressure 125/80 The right renal region and right upper quadrant were tender Laboratory data Hemogram normal, urea-nitrogen in blood 20 mg per 100 cc, clear urine with pH 5 5, specific gravity 1 008, albumin 0, sugar 0, and rare leukocyte per high power field of unspun sample Urine culture contained hemolytic Staphylococcus albus which was sensitive to several antibiotics, stools had no amebae Radiographic data excretory urography showed normal left kidney but marked right hydronephrosis (fig 3), both kidneys were normal in position and were not abnormally mobile, chest and barium enema were negative Cystoscopy showed normal bladder and urethra Catheters (5F) were introduced easily into each renal pelvis, urine from each was not abnormal by urinalysis and was bacteria-

Accepted for publication June 29, 1955
Read at meeting of Intercity Urological Society February 21, 1955, at the Riveroaks Country Club, Houston, Texas, through courtesy of Dr J R Blundell



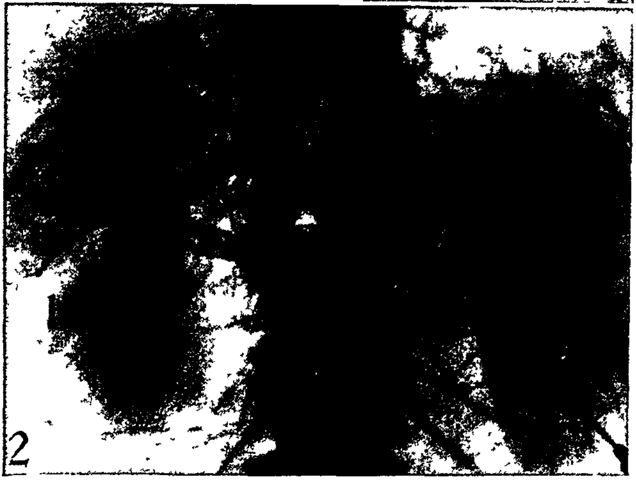
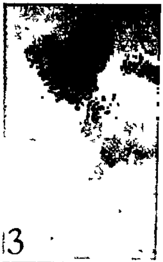


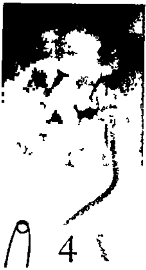
FIG. 1. Case 1. Preoperative retrograde pyelogram. Residual barium is present in colon from previous barium enema.

FIG. 2. Case 1. Preoperative aortogram. Left renal artery and its branches are normal. Right renal artery shows wide bifurcation, *b*, close to renal hilum, both branches entering kidney through hilum.

free. Retrograde pyelography disclosed normal left kidney and ureter but advanced right hydronephrosis with obstruction at upper ureter (fig. 1). Aortogram (fig. 2) showed wide bifurcation of the right renal artery, *b*, the lower branch of which was suspected of being, indirectly, the offending agent. There was no wide bifurcation of the left renal artery (fig. 2). Radiographic sectional areas of the lumen of the proximal 3 cm. of each renal artery were approximately equal, as measured with planimeter: the right being 2.18 sq. cm. and the left 1.90 sq. cm.

Findings at surgery: The parenchyma was normal in color and consistency and questionably subnormal in thickness. The pelvis was large and bulging. Pelvis and upper ureter were slung anteriorly over the lower polar branch of the renal artery (fig. 12, *C* and 13, *A*). Shutting off the lower polar artery, by a rubber-shod intestinal clamp, produced sharply demarcated pallor of the lower third of the kidney. There was no other extrinsic obstruction. Careful mobilization of pelvis and upper ureter resulted in collapse of intact pelvis and reduction in size of kidney (fig. 12, *D* and 13, *B*). Forty cubic centimeters of saline, injected by needle into the pelvic lumen, were immediately transmitted down





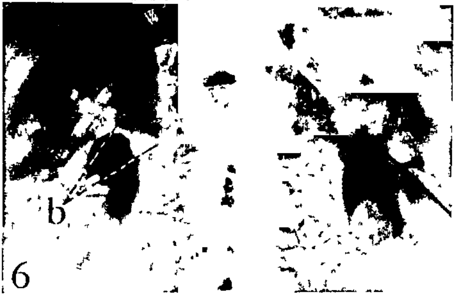


FIG. 3. Case 1. Preoperative excretory urogram of right kidney 40 minutes after injection of iodide. Note markedly swollen calyces and distended pelvis

FIG. 4. Case 1 Postoperative pyelogram of right kidney; twentieth postoperative day. Contrast medium was injected through indwelling 16F pyelostomy tube and was thoroughly mixed with urine in pelvis such that net amount of fluid added to pelvis was nil. Note ureter well injected in lower portion of radiogram.

FIG. 5. Case 1 Postoperative excretory pyelogram of right kidney. Six months postoperatively.

FIG. 6. Case 1. Postoperative combined aortogram and retrograde pyelogram. Twenty-sixth postoperative day

the ureter by fluid wave and visible perstalsis of pelvis and ureter. This demonstrated absence of intrinsic obstruction. The impedance had obviously been compression of upper ureter between distended pelvis and lower polar artery.

Procedure: With the patient in left decubitus and right flank hyperextended, a subcostal lumbar incision was carried through the external oblique, internal oblique, and transverse muscles. The lumbodorsal fascia was entered through the superior lumbar triangle after deflecting the lateral border of the latissimus dorsi posteriorly. Gerota's fascia was incised and the kidney mobilized. Fascia was dissected from the anterior surface of the renal pelvis. The cephalic portion of the ureter was identified and tagged by umbilical tape. The lower polar artery which entered the renal hilum was carefully mobilized. There was no other extrinsic obstruction. Pelvis and upper ureter were mobilized, resulting in active contraction of pelvis. The lower polar artery was then allowed to slide up the anterior surface of the pelvis (figs. 12, *D* and 13, *A* and *B*) and was fixed by sutures of 5-0 chromic catgut, swaged to a round minimal trauma needle, to the cephalic portion of the anterior wall of the pelvis and to the adventitia upper branch of the renal artery (figs. 12, *D* and 13, *B*). The hernial defe thus closed. A 16F two-winged latex catheter was introduced into the pelvis through the posterior surface of the latter (fig. 13, *B*) and brought the posterior angle of the body-wall incision. This catheter was fixed pelvis with a suture of 5-0 chromic catgut. Gerota's fascia was sutured b the lower pole of the kidney to the fascia of the psoas muscle. The kidne partially decapsulated to aid fixation. A fine ribbon-rubber drain was b out at the posterior angle of the wound. The pyelostomy tube was sutured skin with silk. A gauze dressing and adhesive tape were applied and th fixed to the dressing by tape and safety pins.

Pyelostomy drainage was used for the following reasons: 1) to keep the decompressed during healing of the repaired hernial gap between the bifur of the renal artery; 2) to act as a nephropexy; 3) to permit a pyelogram end of 3 weeks (fig. 4) and thus to show degree of regression toward nor the pelviocalyceal system, and 4) to demonstrate absence of pyelou obstruction prior to removal of the tube.

Fixation of the kidney was considered necessary because of increased mobility after mobilization and because of a somewhat redundant urete parent increase in length of ureter was probably due to prolonged stretch o through the hernial gap (figs. 12, *A* to *C* and 13, *A* and *B*). Fixation wa duced thus: 1) indwelling pyelostomy tube for 3 weeks; 2) renal decapsul 3) tacking the perirenal fascia beneath the lower pole of the kidney; a maintaining the patient constantly in the head-down position during th fourteen postoperative days.

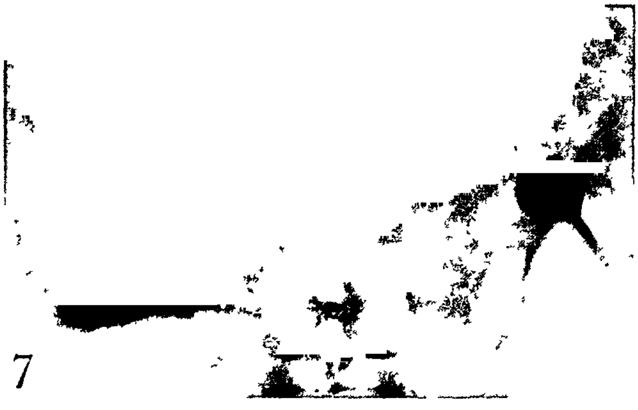
The pyelostomy tube, apart from its virtues, is a conduit of infection the exterior. In future, similar, uninfected cases, pyelostomy may be on but formal high nephropexy performed.

The postoperative course was smooth. On the sixth day, the 2-hour pl sulfonphthalein excretion was 20 per cent through pyelostomy tube and 4 cent through urethral catheter. On the seventh day the dressing was first cha the skin clips removed, and the ribbon-rubber drain pulled 3 cm. The was removed on the tenth day. An antegrade pyelogram, through the p tomy tube on the twentieth postoperative day, was obtained by gently flu the pelvis with 30 per cent skiodan* and the tube was not clamped. The was normal and the calyceal fornices were sharp (fig. 4). Skiodan had en the bladder. The pyelostomy tube now was removed. The pyelocutaneous closed promptly and the patient remained afebrile. Combined retrograde lography and aortography were performed on the twenty-sixth postope day (fig. 6). The pyelogram of the right kidney appeared normal and ide with that of the left (fig. 6). The two branches of the right renal artery, had been exceptionally wide apart preoperatively, were now close tog (fig. 6, *b*). All visible branches of the right renal artery were closer tog than during the preoperative, hydronephrotic state. Urine from the right k

* Sodium mono-iodomethanesulfonamide of Winthrop.

contained Aerobacter which was sensitive to chloromycetin, furadantin, and polymyxin. Although the patient remained afebrile he was given chloromycetin and furadantin for 8 days. Now, 9 months postoperatively, he is symptom-free and his right kidney appears normal by excretory urography (fig. 5).

Case 2. (VAH 45186), a 25-year-old Caucasian man was admitted with chief complaint of pain in the right lower quadrant and nausea. He had been well until the age of 13, when he first had pain in the right lower quadrant radiating laterally. The recurrent pain was dull and severe, lasting about two days and accompanied, at onset, by vomiting. At about the age of 15 he was free of pain for a year, after which the pain recurred often until the age of 18. It then subsided in frequency, appearing only after drinking. At 21, while in Korea, the pain recurred severely and lasted several days. He was seen by a neuropsychiatrist. On the trip home he had several attacks. The pain disappeared for 3 years but recurred frequently at 24. The patient volunteered the information that he did not "drink" because of ensuing pain in his right side. During attacks he had pollakiuria but no dysuria. His history by systems was otherwise negative. He was slender, well developed, and well nourished. On admission his oral temperature was 98.6F, pulse 90 per minute, and arterial pressure 130/90. Physical examination showed only tenderness in the right renal region. During his preoperative hospitalization he had recurrent low grade fever (about 99.6F) in the afternoons. Laboratory data: Hemogram normal; clear urine at pH 4.8 with sp. gr. 1.020, albumin 0, rare leukocyte per high power field of unspun sample; urine culture negative. Radiographic data: Chest and barium enema negative; excretory urography demonstrated normal left kidney and marked right hydronephrosis (fig. 9). Cystoscopy showed no significant abnormality of bladder or urethra. Catheters (5F) were passed readily into each kidney. Five cubic centimeters of 30 per cent skiodan were injected into the left pelvis and 40 cc into the right pelvis after aspirating 50 cc of clear urine from the latter (fig. 7). Urine from each kidney was negative microscopically and by culture. An aortogram superimposed upon a retrograde pyelogram implicated obstructing lower polar artery (fig. 8, *p*). A right "pyeloplasty" was done. In contrast to case 1, the renal parenchyma was distinctly thinned. Such was borne out by the marked disparity in the radiographic sectional areas of the lumen of the proximal 3 cm. of the right and left renal arteries as measured by planimeter (1.3 sq. cm. and 2.3 sq. cm., respectively). Careful mobilization disclosed the enormous pelvis and the cephalic portion of the ureter extruding through a gap between a bifurcation of the renal artery (fig. 13, *A*). In case 2, however, there was a moderately large vein (fig. 13, *A*, *r*) contiguous to the polar artery, *lp*. The right testicular vein, *tv*, joined the lower polar vein. After mobilization, the pelvis collapsed by propelling urine down the ureter and the kidney diminished in size (fig. 13, *B*). Repeated distension of the pelvis with saline, through a needle, caused prompt peristalsis of pelvis and ureter. A 10F catheter could readily be passed down the ureter through the small pyelotomy. Clamping the lower polar artery plus vein, with a rubber-shod intestinal clamp, resulted in cyanosis throughout the caudal third of the kidney, *y*, indicating that the vein drained more parenchyma than was supplied by the artery. It



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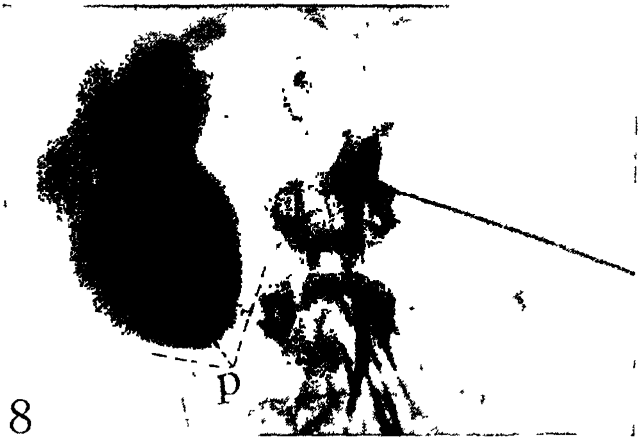

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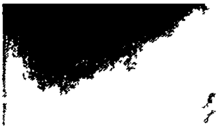

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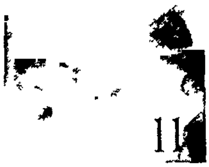

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FIG. 7. Case 2. Preoperative retrograde pyelogram after withdrawal of ureteral catheters. Skiodan (5 cc of 40 per cent) injected into left renal pelvis and 40 cc of 40 per cent skiodan into right renal pelvis after aspiration of 50 cc of clear urine from latter.

FIG. 8. Case 2. Preoperative aortogram combined with retrograde pyelogram. Polar artery, *p*, to right kidney.

FIG. 9. Case 2. Preoperative excretory pyelogram of right kidney showing moderate recession of hydronephrosis during dehydration but continued marked ballooning of calyces. Poor concentration.

FIG. 10. Case 2. Postoperative pyelogram of right kidney; twenty-fourth postoperative day. Skiodan injected through indwelling 16F pyelostomy tube in same manner as for case 1 (see legend for fig. 4).

FIG. 11. Case 2. Postoperative excretory pyelogram of right kidney. Five months postoperatively. Note funnel-shaped pelvioureteral junction.

was necessary to divide the testicular vein (fig. 13, *B*, *tv*) to lift the lower polar artery and vein in their common sheath and suture them to the superior mainstem artery and to the upper, i.e., cephalic surface of the renal pelvis. Adventitia was not stripped from these vessels because it was used to hold the sutures. Es-

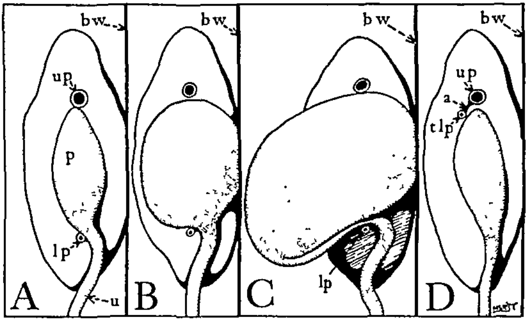

FIG. 12. Stages in presumed development of hydronephrosis secondary to polar or aberrant vessel(s). Kidney is viewed from medial aspect; renal pelvis and ureter are stippled. This may occur during embryonic life but is more likely during postnatal growth. *bw*, posterior body wall; *lp*, lower polar artery to kidney; *p*, renal pelvis; *u*, ureter; *up*, upper polar artery.

A, presumed initial state; *B*, beginning bulge of pelvis anteriorly, between renal arteries; *C*, advanced bulging of pelvis anteriorly resulting in compression of ureter and in false impression of "retropelvic vessel;" *D*, reversal to presumed initial state with recovery from obstruction by mobilizing pelvis and upper ureter and transposing lower polar artery cephalad, *tlp*, and closing hernial defect between arterial bifurcation by apposition of respective adventitiae, *a*.

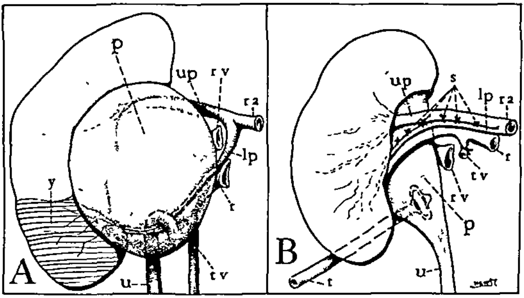

FIG. 13. Case 2. *A*, anatomical relations of right hydronephrotic kidney as seen during surgery. *lp*, Lower polar branch of renal artery; *p*, greatly distended renal pelvis; *r*, lower polar branch of renal vein accompanying polar artery; *ra*, mainstem renal artery; *rv*, main renal vein; *tv*, right testicular vein entering lower polar renal vein, *r*; *u*, ureter; *up*, upper branch of renal artery Region of kidney, *y*, which became cyanotic upon clamping both *lp* and *r*, is indicated by horizontal lines.

B, condition of *A* at close of surgery. *lp*, Lower polar renal artery; *p*, collapsed renal pelvis; *r*, lower polar renal vein; *ra*, main-stem of renal artery; *s*, fixation sutures maintaining cephalic transposition of *lower* polar artery; *t*, pyelostomy tube, 16F; *tv*, divided and ligated right testicular vein; *up*, upper polar renal artery.

sentially the same procedure was performed as in case 1. Nephropexy was by pyelostomy tube (fig. 10). The ureter was more redundant in case 2, after mobilization, than in case 1. Postoperatively the patient was kept in the head-down position for 14 days. On the twenty-fourth day a pyeloureterogram through the pyelostomy tube showed satisfactory communication between pelvis and ureter and also indicated extent of regression of pelvis and calyces toward normal (fig. 10). The same technique for obtaining such a pyelogram was used as already described for case 1. The pelvis was then irrigated with neomycin solution (5 mg. per cc) and the pyelostomy tube removed. The pyelocutaneous tract closed promptly and the patient remained afebrile. The following day his urine showed pH 5.0, sp. gr. 1.018, albumin trace, and 7 to 9 leukocytes with few bacteria per high power field of unspun sample. Urine culture yielded Aerobacter sensitive only to furadantin and polymyxin. He was given polymyxin (2.5 mg. per kg. per 24 hours) intramuscularly and furadantin 100 mg. 4 times daily orally, both for 7 days. After starting this medication he underwent a daily febrile spike which subsided promptly and definitively at the close of this course of antibiotic therapy. He remains renally asymptomatic several months after discharge. His excretory urogram continues to show maximally regressed hydronephrosis and an excellent dependent funnel at the pyeloureteral junction (fig. 11). Aortogram performed akout 8 months postoperatively (not shown here) indicates that the angle of bifurcation of the right renal artery has been greatly narrowed.

DISCUSSION

1) *Hydronephrosis secondary to large urinary flow.* Hydronephrosis literally means "water-kidney" and is defined as "dilatation of the pelvis and calyces of one or both kidneys in consequence of obstruction to the flow of urine."* Literal hydronephrosis and hydroureter, however, can occur in an entirely normal urinary tract upon intake of a large volume of water. Covington and Reeser ('50) reported a young man who had intermittent pain in the right lower quadrant precipitated, in all instances, by excessive ingestion of fluid such as several bottles of beer. Excretory urography disclosed prominent right hydronephrosis after he drank 1500 cc of water, but normal right kidney after routine dehydration. A small obstructing vessel was divided. Postoperative excretory urogram with overhydration was said to be normal.

We have found that forced diuresis (2,000 cc of water in 2 hours immediately preceding excretory urography) caused distension of the entire calyco-pelvio-ureteral system in the twelve young men with normal urinary tracts which were tested (e.g., figs. 14 and 15). Excretory urograms, using 25 cc of 70 per cent "urokon" (Na 3-acetylamino-2,4,6-tri-iodobenzoate), showed calyceal blunting (fig. 14, *D* and *H*; 15, *A* and *B*). One subject had had a V-Y plastic relief of a congenital intrinsic pyeloureteral obstruction, which indicated excellent result by routine dehydration (fig. 14, *A*) but showed advanced blunting of the calyces during forced diuresis (fig. 14, *B*). During excretory urography the bladders of these patients were kept empty by indwelling plain catheters taped to the penis. Relation of diuretic pelvic dilatation to the concept of acquired hydronephrosis is indicated below.

2) *Acquired hydronephrosis.* The term "intermittent hydronephrosis" (Israel, '01; Bazy, '03; Braasch, '09; Jones, '09) antedates excretory urography and

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* Stedman's Practical Medical Dictionary. 1946, Williams & Wilkins Co., N. B. Taylor ed.

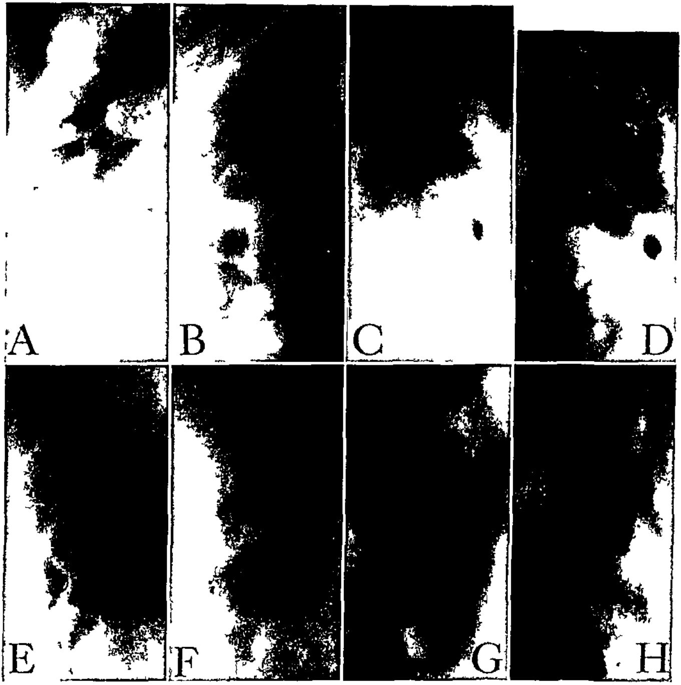

Fig 14 Excretory urograms of normal kidneys of young men during dehydration (antidiuresis) and forced diuresis A
(VAH 28577), B and D, diuretic righ
antidiuretic right and left kidneys, r
left kidneys, respectively (VAH 29774)

riginates from the intermittent pain There is little evidence that the hydro-
ephrosis, as such, was intermittent although this was often assumed Israel
01) reported disappearance of a hydronephrotic mass upon abdominal palpa-
on and noted that some patients learned thus to reduce such masses and obtain
mptomatic relief Lower polar arteries are not infrequently implicated in
ntermittent hydronephrosis" of adults (Mayo et al, '09, Jones, '09, Moore,
7) Partial occlusion of the upper ureter between renal pelvis and lower polar
ery is the commonest cause of hydronephrosis producing first symptoms
ing young adulthood (Mayo et al, , Winsbury-White, '25, Moore, '37).
Iydronephrosis implicated by aberrant or by lower polar renal artery appears
e acquired usually during postnatal growth rather than to be congenital
s is suggested by a) low incidence in infants (see below) and b) usual ab
e of symptoms until young adulthood

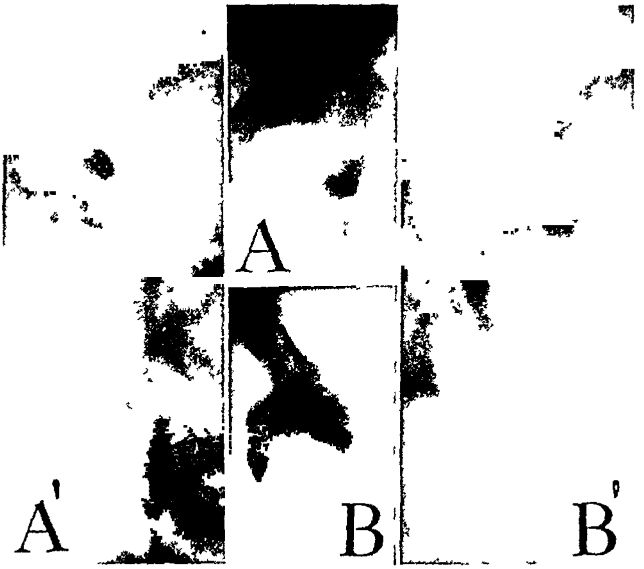

FIG. 15. Excretory urograms of normal kidneys of young man (VAH 50572) during dehydration (antidiuresis) and forced diuresis. *A* and *B*, right and left kidneys, respectively, during dehydration (antidiuretic); *A'* and *B'*, same kidneys during diuresis

a) Incidence of hydronephrosis with obstructing vessels in infants: Bugbee and Wollstein ('24) reviewed 4903 necropsies of infants and found 44 cases of hydronephrosis. The obstruction was identified in most cases. In none of these was a vessel implicated. Although hydronephrosis was the commonest congenital anomaly of the urinary tract in infants, obstruction at the ureterovesical junction or in the urethra was the commonest cause. Lower polar artery without associated hydronephrosis, nevertheless, is common in children (White and Wyatt, '42) and hydronephrosis secondary to upper ureteral obstruction by a lower polar artery is not unknown in infants (White and Wyatt; Campbell, '51; Gross, '53). Campbell reports advanced hydronephrosis secondary to obstructing vessels in young children. Gross found vessels implicated in 44 out of 156 pelvioureteral obstructions in patients below the age of twelve. Stewart ('47) pointed out that as the child grows the kidney opens out like an efflorescent bud and that if a lower polar artery is present in infancy it will be close to the main renal artery and thus be unlikely to produce obstruction at that stage.

b) Age of onset of pain and vomiting is usually in young adulthood (Braasch, '09; Mayo et al. '09; Hutchinson, '13; Winsbury-White, '25; Mathé, '28). The pain may be confined to the lower quadrant and, if right-sided, may simulate appendicitis, as in case 2. The appendix has been removed often without cessation of symptoms (Braasch, '09; Campbell, '51). Intermittency of attacks may be spaced in months or years, but its frequency usually increases (Hutchinson).

3) Herniation of the renal pelvis. The hilar branches of the renal artery are often exposed beyond the margin of the renal pelvis (Anson and Kurth, '55). This is probably the basic "defect" permitting upper ureteral obstruction. The renal vein, on the other hand, usually receives its renal tributaries close to or within the renal hilum. Bazy ('03) and Legueu ('04) suggested that flexure of the ureter over a vessel is secondary to pelvic dilatation In advanced cases the ureter may be strictured at the site of compression (Jones, '09, Mayo et al '09, Winsbury-White, '25, Mathé, '28) Winsbury-White dissected several specimens of hydronephrosis implicated by a lower polar artery and found that the renal artery typically proceeds to the upper part of the hilum and there divides into three main branches two superior and one inferior The inferior vessel resulted in compression of the upper ureter during pelvic distension He suggested that the dilating pelvis expands anteriorly in the direction of least resistance It may bulge through an extrahilar bifurcation of the renal artery and/or vein, drawing the ureter with it (fig 12, *A–C*) hence the erroneous theory of hydronephrosis due to a "retropelvic artery" (Eisendrath, '20) or "anomalous vessel" passing behind the pelvis (fig 12, *C, lp*) In none of the specimens was the artery implicating the ureter "aberrant", that is, the artery entered the kidney by way of the hilum and not through the cortex In all but two of 20 cases with obstructing polar artery, the latter was a branch of the main renal artery (Mayo et al, '09)

Given the anatomical defect of a wide extrahilar bifucation of a major renal vessel and given that a large intake of water results in pelvic dilatation even in a normal pelvioureteral system (see above), it appears probable that the pelvis, during dilatation, distends the thin fascia between the bifurcating renal vessel and may finally break through as a fully blown hernia or acquired hydronephrosis

Hydronephrosis implicated by a lower polar artery may occur significantly more often on the right side than on the left (Braasch, '09, Hutchinson, '13) but White and Wyatt ('42) report involvement of the right in twelve cases and of the left in seventeen Because this hydronephrosis occasionally has been seen in an advanced state in infants (Campbell, '51) and because the metanephros functions early during fetal development (Windle, '40), it appears that herniation of the renal pelvis may occur, although rarely, even during embryonic life

4) Treatment of hydronephrosis implicated by lower polar artery Eisendrath ('27), Patch ('29), and O'Conor ('55) warn against sacrificing the lower polar artery, which may result in perinephric abscess from ischemic necrosis of a renal segment Possibility of ensuing hypertension, furthermore, has not been excluded for all cases Campbell ('51) states that if the ischemic area is greater than 25 per cent of the renal surface the polar artery should not be divided O'Conor ('55) notes that sacrificing the polar artery is safe only with a kidney which has a central arterial supply Gross ('53) favors division of the polar ("aberrant") artery Quinby ('27) and Ormond ('37) practiced reimplantation of ureter into pelvis Patch ('29) reimplanted the ureter along with a cuff of pelvis Neither Quinby nor Patch used splints and success was claimed but excretory urography was not available Young ('32) suggested resection of pelvis such that the reconstruction would draw the ureter away from the vessel Campbell ('51) states that "occasionally free mobilization of the ureteropelvic junction and high nephropexy will suffice" Since the hernial defect is not repaired recurrence may be likely Stewart ('47, '54) presented an ingenious and highly effective method which attempts to re establish the anatomical relationship of infancy by closing the gap between the main renal vessel and the lower polar vessel.* Our method utilizes the converse of the same principle, that is, after mobilization of pelvis and upper ureter, the gap between the bifurcating vessel (figs. 12, *D* and 13, *A*) is closed by primary apposition of the vessels (fig. 13, *B*) rather than by primarily approximating the opposite poles of the kidney. We do not claim that our method would be applicable to all cases implicating polar vessels. Careful mobilization of pelvis and upper ureter would indicate its feasibility in a given case. The pyeloureteral junction should be checked for possible obstruction, as described under Methods. Advantages of Stewart's method and of the present are: 1) pyeloureteral continuity is maintained; 2) polar vessels are not sacrificed; and 3) the anatomical "defect" is repaired.

SUMMARY

It is shown that the calyco-pelvio-ureteral system of a completely normal urinary tract will undergo dilatation during forced diuresis.

It is postulated that dilatation of an extrarenal pelvis may lead to its herniation within a wide extrahilar bifurcation (the anatomical "defect") of the main-stem artery and/or vein and thus result in acquired obstruction of the upper ureter.

A method is presented for relief of obstruction secondary to compression of upper ureter between dilated pelvis and lower polar artery. Mobilization of pelvis and upper ureter is followed by closure of the hernial defect by suture-juxtaposition of the lower polar vessel to the main-stem vessel and to upper, i.e., cephalic, surface of renal pelvis.

This method avoids severing nutrient vessels and mutilation of continuity between pelvis and ureter. The method assumes that intrinsic obstruction at pyeloureteral junction has been looked for and found absent.

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THE JOURNAL OF UROLOGY
Vol. 75, No 2, February 1956
Printed in U.S A

METASTATIC CARCINOMA OF THE URETER

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The ureter is not uncommonly involved in malignancy by direct extension from a primary tumor. This is frequently seen in carcinoma of the cervix which characteristically spreads along the broad ligament to entrap the lower ureter. Primary tumors of the ureter as well as those resulting from spread along the urinary tract are occasionally seen, but a review of the available literature shows that the ureter is only rarely the recipient of genuine metastatic tumors. Thirty-four cases involving the breast, lung, stomach, bowel, prostate, urethra, ovary, uterus and vagina as the primary site have been reported, but we have been able to find only cases reported by Carson, Drexler, and MacKenzie and Ratner in which carcinoma of the cervix spread by metastasis to the ureter, and add the present case making a total of four.

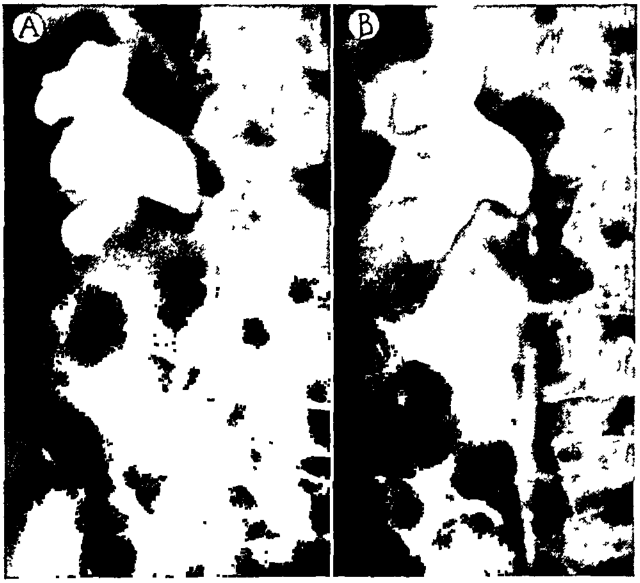

FIG. 1. *A*, pyelogram shows only hydronephrosis. *B*, pyeloureterogram shows filling defect in upper ureter.

A 48-year-old white woman was seen in our clinic because of 5 days of constant dull aching pain in the right flank. She denied any urinary symptoms or fever, but had been nauseated and had vomited several times in the past 2 days.

Her past history revealed that she had been treated with radium therapy 1 year earlier for epidermoid carcinoma of the cervix, grade 2, stage 2; retrograde pyelography at that time was normal. Pelvic examinations subsequent to her therapy failed to disclose evidence of recurrence of the carcinoma. Physical examination revealed only right renal tenderness. Blood count, nonprotein

Accepted for publication July 28, 1955.

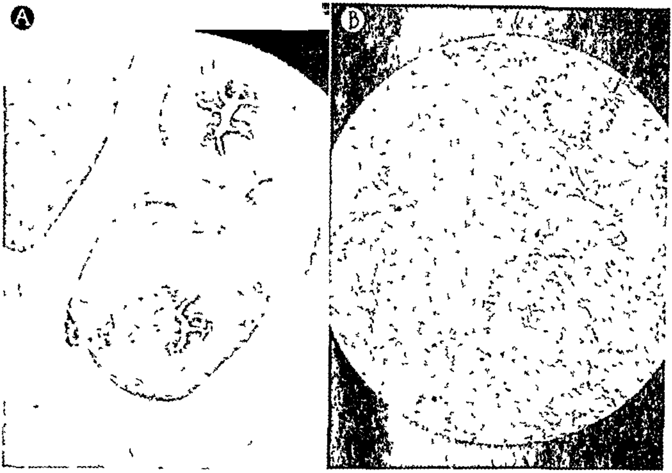

FIG 2 *A*, low power magnification of tumor bearing ureter *B* same area, high power, showing typical epidermoid tumor

nitrogen and urinalysis were normal as was the chest x-ray An excretory urogram showed no function from the right kidney at the end of 2 hours. The left pyelogram was normal A right retrograde pyelogram was done (fig 1, *A*), and an obstruction was met and passed by the catheter about 20 cm up the ureter. The withdrawal film (fig 1, *B*) clearly demonstrated a 3 cm filling defect in the proximal ureter between the second and third lumbar vertebrae Exploration of the ureter showed this to be due to a dense sleeve of tissue which encompassed the ureter and was adherent to the fascia and the vena cava A frozen section was reported as carcinoma and a nephroureterectomy was done Permanent sections from the ureter (fig 2) establish the diagnosis of epidermoid carcinoma.

SUMMARY

An unusual case of metastatic epidermoid carcinoma from the cervix to the ureter with resultant hydronephrosis is presented A survey of the literature reveals this to be the fourth such case reported

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

ELECTROPOTENTIAL CHANGES IN THE NORMAL HUMAN URETER

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In a series of studies from these laboratories, electromyographic records from the urinary bladders of six mammalian forms including man[1, 2, 3] have been described. Limited observations on isolated sections of human ureter obtained during surgery[2] indicated that the electroureterogram, as we have recorded it, closely resembled the electrocystomyogram in general characteristics. This observation has led to the present report, which concerns a further investigation of bioelectric activity within the normal human ureter in situ.

METHODS

Female patients without demonstrable urinary tract disease were selected for study. Demerol (75 mg.) sedation was used to minimize pain and consequent muscular movement during the recording period. The knee-rests of the cystoscopy table were padded with sponge rubber to assure maximal comfort, and particular effort was made to maintain a reassuring atmosphere of calm and quiet in the examining room, in which subdued lighting was used. No patients were included in this study in whom apprehension or discomfort was apparent on passage of the electrodes.

The ureteral electrode was made up to our own design* (fig. 1). Essentially, it is similar to one described by Milton and Robb[4], consisting of a No. 6 nylon ureteral catheter fitted with two silver ring-electrodes. The distal ring is 3 cm. from the tip, a space of 5 cm. separating the two electrodes. The instrument contains an open channel in order to prevent ureteral obstruction with resultant stretching of the musculature by the accumulation of urine. This technique cannot, however, eliminate a certain minimal degree of ureteral stretching due to the presence of the catheter itself within the ureteral lumen. The electrical connections as well as the open channel, or lumen, terminate in a plastic fitting at the end of the catheter proximal to the operator. In use, this electrode-carrier was inserted into the ureter through the cystoscope for a distance of 20 cm. A silver ground connection was placed on the patient's abdomen in the midline approximately 5 cm. above the umbilicus, and held in place by strips of adhesive

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Accepted for publication July 29, 1955.

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* The special electrode-carrier was furnished through the co-operation of Mr. Frederick J. Wallace of American Cystoscope Makers, Inc., New York, N. Y.

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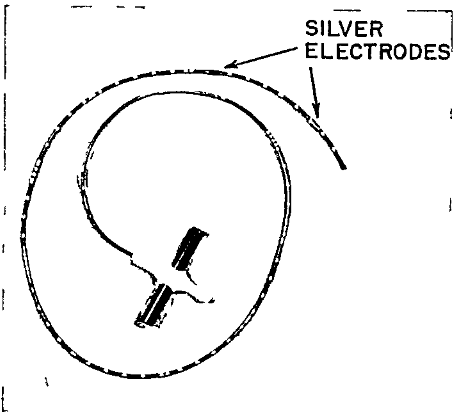

FIG 1 Ureteral electrode used in conjunction with Grass oscillograph Silver ring electrodes are mounted on No 6 nylon catheter Distal electrode is 3 cm from catheter tip and distance of 5 cm separates electrodes Instrument contains an open channel to minimize stretching of the ureter by accumulated urine during recording period

tape Electropotential differences between the ring electrodes were recorded on a Grass ink-writing oscillograph,* at a paper speed of 15 mm /sec

For purpose of comparison, electromyograms from a series of 7 ureteral sections (av length 4 cm) obtained from the operating room were recorded according to a technique previously described [9]

RESULTS

Representative electromyograms from the 8 patients are shown in figure 2, while frequency of contraction, and the average duration and electropotentials developed are presented in table 1 The graphic similarity of these tracings to those obtained from the urinary bladder in earlier studies [1 2 3] was striking, and we have, therefore, characterized the various deflections as "a", "A", "B" and "b" waves in conformity with the nomenclature which we initially adopted in descriptions of electromyograms obtained from that viscus It was observed that respiratory movements which may at times seriously distort records from the bladder did not affect any of the ureteral records On the other hand, supposedly mechanical artefact was frequently seen due to impulses transmitted from the beating heart These may be seen in tracings E and F

Periods of activity tended to alternate with quiescence, although this was not always observed In the record from patient H a marked tendency for the waves to appear in pairs was quite striking, such pairs of deflections occurring without a perceptible pause between the two components Only in patient A were "a" de

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* The writers wish to express their appreciation and thanks to Dr J W Crosson of the C D Searle Co , Chicago Illinois for support making possible the purchase of the special Grass oscillograph used in this and other studies

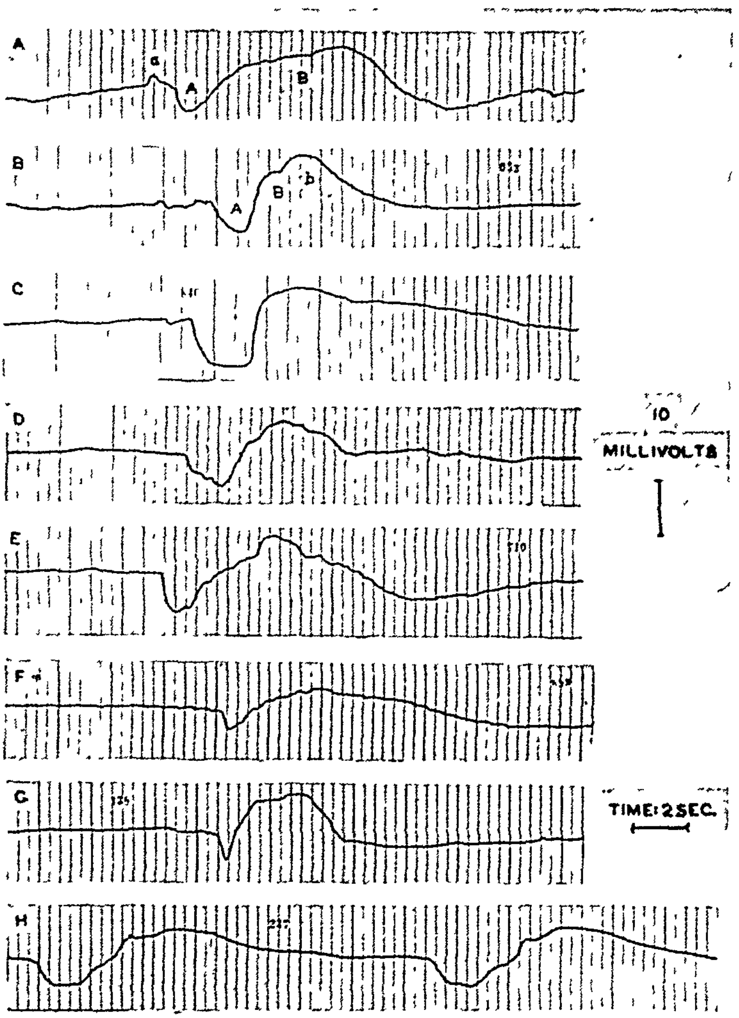

Fig. 2. Representative records obtained from 8 female patients without demonstrable urinary tract disease. Various deflections of typical tracings have been arbitrarily designated "a", "A", "B", and "b" deflections.

flections uniformly present—a wave form which we have considered to be characteristic of the bladder.

In all cases, the very high potentials developed were most striking, the voltages being of approximately 10 times the magnitude of those recorded from the urinary bladder.[1]

In general, however, no variations in the form of the records obtained served to differentiate them from electromyographic tracings obtained from the bladder in situ. The duration of the potential shifts was, however, approximately twice that seen in the bladder.[1]

When the above myograms were compared with those obtained from a series of ureteral strips (fig. 3), the striking similarity in both wave form and in average frequency of contraction was at once apparent (ureter in situ: 2.47 per min.; ureteral strips: 2.49 per min.). It hence appeared that frequency of ureteral activity is independent of an intact innervation. As might be anticipated, electro-

TABLE 1. *Characteristics of bioelectric activity recorded from the human ureter*

Subject	Age (yrs.)	*Pathology*	Frequency/ min.	Average Duration of *Potential* Change (sec.)	Average Duration of "A" Wave(sec.)	Average Duration of "B" Wave(sec.)	Average EMF *"A"* Wave (Mv)	Average EMF *"B"* Wave (Mv)
A	39	Stage I carcinoma of cervix	2.40	6.90	1.34	5.56	4.25	6.65
B	41	Stage I carcinoma of cervix	2.40	7.49	1.83	5.66	3.18	5.56
C	41	Stage I carcinoma of cervix	2.90	11.20	3.60	7.60	10.60	10.60
D	46	Stage I carcinoma of cervix	2 80	8.72	2.58	6.14	4.51	4.16
E	50	Stage I carcinoma of cervix	2.55	8.84	1.86	6.98	3.28	5.33
F	53	Stage I carcinoma of cervix	2.60	11.75	2.35	9.40	4.00	8.25
G	59	Stage I carcinoma of cervix	2.20	4.90	0 78	4.12	3 71	6.36
H	67	Uterine fibroid	1.90	10.75	1.35	9.40	2.10	2.49
Average..	49.5		2.47	8.82	1.96	6.86	4.45	6.18

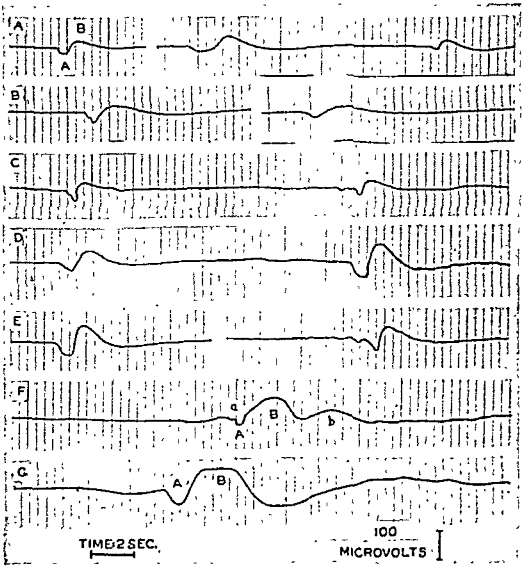

FIG. 3. Typical records recorded *in vivo* from isolated ureteral sections obtained at operation. Marked similarity between these records and those shown in figure 2 is clearly apparent.

TABLE 2. *Characteristics of electromyograms secured from isolated ureteral sections*

Section	Frequency/min.	Average Duration of Potential Change (sec.)	Average Duration of "A" Wave (sec.)	Average Duration of "B" Wave (sec.)	Average EMF "A" Wave (μv)	Average EMF "B" Wave (μv)
A	2.5	3.02	0.82	2.20	18.8	22.5
B	2.5	2.82	0.72	2.10	26.1	45.0
C	2.4	4.10	1.10	3.00	22.5	27.5
D	2.8	2.74	0.94	1.80	30.0	25.0
E	2.6	3.65	0.45	3.20	17.5	16.3
F	2.1	5.50	1.00	4.50	35.0	55.0
G	2.5	3.60	1.40	2.20	17.0	27.0
Average........	2.49	3.63	0.92	2.71	23.8	31.2

potentials developed within the isolated sections of ureter were much reduced. Thus, the average, maximal "B" wave potential exhibited by the intact ureter was 198 times as great as that developed by the ureteral strips. Further, the duration of potential change in situ averaged 2.43 times that in the tissue samples. See table 2.

DISCUSSION

Hanley[5] and Milton and Robb[4] have described electroureterograms obtained from human subjects by techniques very similar to that which we have employed. It is interesting to observe that their records are, in main essentials, similar to those which we obtain. The "pressure waves" observed by Hanley "last about nine seconds," while the total duration for a complete wave of activity averaged 8.82 sec. in our subjects.

The uniformity of frequency of the waves of ureteral activity is striking. Thus, in the 7 cases of cervical carcinoma, the maximal variation was from 2.2–2.9/min. In the single case of uterine fibroid, frequency was reduced to 1.9/min. Morales, Crowder, Fishman and Maxwell,[6] working with dogs in which the trigone had been surgically exteriorized, found that the "vigor of contractions increased with increased urine flow, but frequency of peristalsis remained constant. . . ." That frequency of contractions in the isolated sections of human ureter is similar to that observed in situ is not surprising in the light of observations by Greene and Essex,[7] who found the dog ureter to be "independent of autonomic connections" and relatively unaffected by drugs. Moreover, Baker and Huffner[8] have observed that sectioning and re-anastomosis of the dog ureter had no effect on the electromyogram. On the other hand Butcher and Sleator have reported the conduction of ureteral peristalsis in the dog to be disturbed following division and re-anastomosis[9].

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The low potentials developed in the excised ureteral sections were quite probably due in large part to leakage through the electrolyte in the water bath. Calafati, Galli and Agnoletto[10] have further observed that the potentials developed by the dog ureter are higher when recorded from internal catheter-mounted ring electrodes than from needles hooked into exposed adventitia.

SUMMARY

A series of electromyograms obtained in situ from patients without demonstrable urinary tract disease is described:

Electromyograms obtained from isolated sections of human ureter are essentially similar to those recorded in situ in their general characteristics as well as in frequency, but of comparatively greatly reduced EMF.

Both of the above types of tracing are strikingly similar in their general characteristics to electromyograms recorded from the human urinary bladder in situ, and in isolated bladder preparations from all of the five mammalian forms which we have studied.

The observations reported adapt themselves, as a normal standard, to further pharmacologic evaluation and studies of ureteral dysfunction.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

THE ELECTROUROGRAM, II. EXPERIMENTAL STUDY

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The first publication on the subject of the electrourogram (EUG)[1] stated that electrical potentials can be traced from the kidneys. The waves recorded, as shown by about 500 electric tracings from the rabbit and human kidney, differ under various physiological and pathological conditions.

This first report on the EUG did not meet with approval or much understanding. Experts either refused to acknowledge the existence of the EUG or considered it as a sort of modified electrocardiogram. It was, therefore, paramount to verify the existence of the EUG by all possible experimental means and to differentiate it from other electrical tracings which might be superimposed on the renal tracings.

Following the nomenclature, tracings from the kidneys are called correctly electronephrogram (ENG). When the electrodes are placed on or inside the renal parenchyma, upon or within the bladder and ureter, the urinary tract as a whole is used for the tracings and therefore the name electrourogram is more appropriate. In fact the EUG comprises the electronephrogram, the electroureterogram, and the electrocystogram, depending upon the position of electrodes on or within the respective organs. It goes without saying that the most important organ for production of potentials is the renal parenchyma. In this experimental study only the ENG will be investigated. This report deals with investigations on rabbits. Human recordings are not included here for the main reason that at the time being new ways of tracings are being tried. Furthermore, experimental work on the ENG of dogs is being done, which considerably differs from the one on rabbits. Further reports shall cover this subject.

TECHNIQUE

A single technique was used consistently during all these experiments. Since the work itself often lasted over 3 or 4 hours, strong, full grown animals, weighing around 3 to 4 kg., were taken. Experience has taught us that, due to their stronger resistance to the strain of the experiments, colored animals are preferable to white ones. The rabbit is narcotized with 60 to 75 mg. of nembutal, depending upon the size of the animal, and administered by the endovenous or intraperitoneal route. If necessary, the amount of nembutal can be increased. The drug must never be injected too rapidly, as the rabbit often reacts to it with cardiac arrest. In order to procure the necessary diuresis, 50 to 70 cc physiologic saline were injected intraperitoneally.

The kidney is exposed in the usual way, retroperitoneally; loss of blood should and can be avoided. Both kidneys can be brought to the surface easily; however, conventionally in our experiments the right kidney was first exposed. The kidney

Accepted for publication July 27, 1955.

[1] Kneucker, A. W.: J. Urol., **69:** 458–461, 1953.

is freed from all surrounding tissue Possible aberrant vessels leading to the upper or lower pole are tied and severed, the kidney pelvis and the ureter freed about 3 cm towards the bladder Similarly, the kidney pedicle is exposed about half an inch away from the kidney Renal potentials and their recordings were taken from the kidney,* from the ureter, from both kidneys simultaneously, as well as from the heart The respiratory curve (pneumogram) is recorded mechanically at the same time, and the latter can exert a considerable and disturbing influence on the ENG

The exposed kidney is wrapped in saline soaked gauze in order to provide a correct contact with the electrodes, application of a lubricant jelly would not be advisable For electrodes small plates, diameter 5 mm , are used which resemble the unipolar chest leads for human beings, when recordings are made from the surface of the kidney, the organ is then sandwiched between the electrodes If potentials from the inside of the kidney are wanted, small needles or hooks are pierced through the renal parenchyma If tracings are recorded from the ureter or the bladder, small wires are introduced into the ureter or the bladder through a very small cystotomy opening, or the wall of those organs can be pierced by the aforementioned hooks About the elastic hanging of the kidney, see later

It must be mentioned that the curves change according to whether the plates or needles are placed opposite from each other on the anterior and posterior side of the kidney, on the upper and lower pole of the organ, or whether one plate is placed on the convexity of the kidney and one needle introduced into the kidney pelvis

For all experiments a Polyviso Sanborn machine permitting four simultaneous recordings is used For scientific purposes it is advisable to use a machine which allows simultaneous tracings of several curves of the same or of different organs, this is the only way for differentiation between ENG and electrocardiogram, ENG and respiratory curves, ENG and electroureterogram, as well as ENG of both kidneys The arrangement of the leads is bipolar, the inactive electrodes are put either into the mouth of the animal or deeply subcutaneously into the incisional wound The speed of recordings is set between 2½ and 25 mm /sec Sometimes a preamplifier was added to one of the channels in order to increase the magnitude of the waves so that 1/10 mv gave a deflection of 1 to 2 5 cm If such a preamplifier is not attached the changes of potentials of parts of the kidneys are occasionally registered with some difficulties

RESULTS

The ENG is first to be differentiated from other potentials as follows

1) ENG and electrocardiogram The ENG and the electrocardiogram were registered simultaneously at a film speed of 25 mm /sec A comparison between the two tracings shows in an unmistakable way that both curves are completely different and present complexes of different rates and rhythms

Moreover, the excised kidney after a nephrectomy was performed keeps

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* Peculiarities of the so called partial potentials of the kidney will be discussed later on

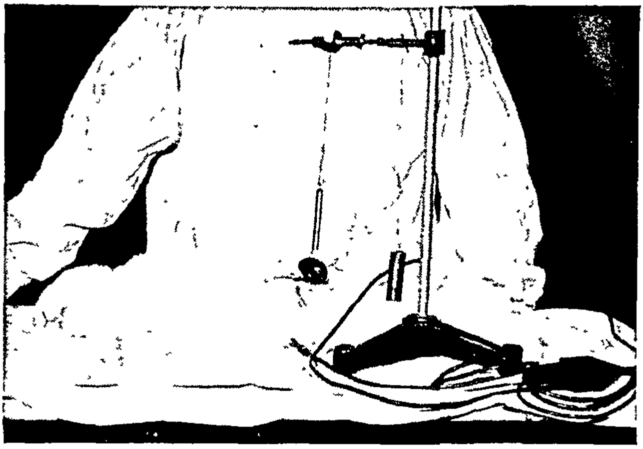

FIG. 1

writing curves for 10 to 15 minutes. It is obvious that the isolated organ cannot give an electrocardiogram.

2) ENG and pneumogram. Under certain circumstances the ENG of the organ in situ records waves which have the same rate as the respiration. These waves are most likely artefacts and due to traction exerted on the kidneys with slight displacement of the electrodes.

There are several ways to differentiate the ENG from the pneumogram.

a. If the exposed kidney is hung on a metallic stirrup which, in turn, is suspended from an elastic spring, movements of the kidney originating from respiration are possible and shifting of the electrodes avoided. Then, changes of renal potential can be traced without interference (fig. 1). When electrical potentials from both kidneys are registered simultaneously, either kidney must be hung in a stirrup.

b. Respiratory curves can also be eliminated by performing a tracheotomy, introducing a small catheter down to the bifurcation of the windpipe, and inflating the lung with oxygen under pressure. Apnea is induced in this way, and the respiratory curve eliminated.*

c. The best method to differentiate between the two curves is by promoting diuresis. About 5 minutes after the injection of normal saline the waves of the ENG begin to increase and to become clearly recognizable both when there were no renal waves before or when they were partially hidden within the pneumogram. The maximal height of the waves is usually reached about 15 to 20 minutes after the injection, at the acme of diuresis.

3) ENG and electroureterogram. When both curves are registered simultaneously, an obvious difference can be noted between the two tracings in regard to height and frequency of the waves. In principle the waves of the electroureterogram are much larger than the renal curves and can be recorded without an amplifier; in fact, however, we have to distinguish between the secretion and

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* M. v. Dungern, quoted in the first publication, was believed to record curves from the kidney which were, in fact, pneumograms, as he obviously failed to know how to deal with the respiratory movements of the animal.

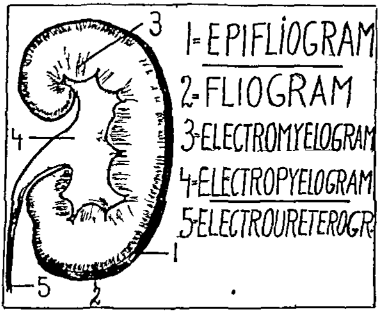

FIG 2

excretion phase ten minutes after the injection of saline the waves of the ENG are larger than the ureter curves, this is the secretion phase performed by the renal cortex and partly by the medulla, which is followed by the excretion phase represented by the tubuli recti, the hollow renal viscus and finally the ureter Which phase is more active is brought to view by the height of the curves When secretion as well as excretion are in full activity, the amplitudes of both curves are about equal

When the changes of potentials of both kidneys are recorded simultaneously the curves are never equal as to shape, amplitude and frequency One curve is always higher which, as already mentioned, shows the greater activity of the organ concerned The other organ seems to rest, however, after some time has elapsed the curves usually change and the formerly resting organ often becomes more active, and vice versa We see that not all glomeruli of one kidney are working simultaneously, and the same holds true for both kidneys

When an excised kidney is dissected by removal of the capsule as well as the hollow viscus from the parenchyma and separation of the medulla from the cortex, it is noticed that separate potentials can be traced from all these parts Applying the proper nomenclature, we can subdivide the electronephrogram into the following parts

a The cortex traces the fliogram *
b The medulla traces the electromyelogram
c The kidney pelvis traces the electropyelogram
d Finally, the ureter traces the electroureterogram

The kidney capsule, being living tissue, traces curves of its own which accordingly must be called epifliogram This epifliogram, however, has nothing to do with the change of renal curves during diuresis and antidiuresis, as could be shown by experiment (fig 2)

Despite a large amount of experiments the mutual relationship between the curves of the partial potentials is not clear It can be said that doubtlessly only

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* Flios (gr) is identical with the Latin word cortex

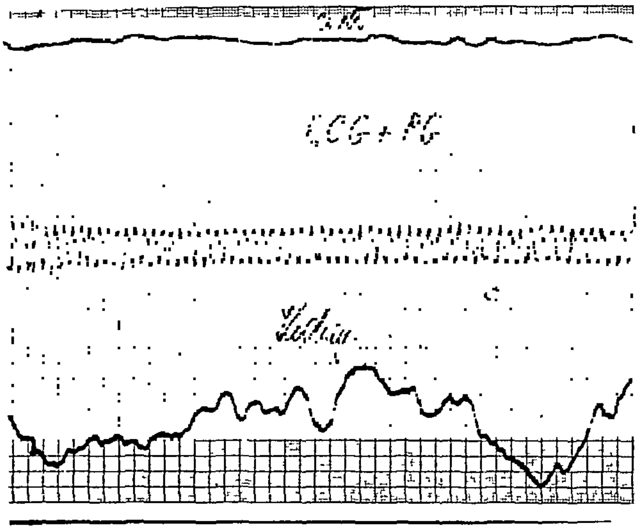

FIG. 3

diogram and electromyelogram play a decisive role in these considerations. All partial potentials combined seem to produce the ENG. The partial potentials seem to act synergistically towards the total potential.

The most important phenomenon of renal physiology is diuresis. As it has been known for a long time, diuresis is achieved by drinking sufficient amounts of water, by injection of normal saline as well as by injection of certain drugs, the so-called diuretics. To decrease the diuresis there are various methods, internal as well as surgical ones. Either pitressin containing the antidiuretic hormone of the neurohypophysis can be injected, or the kidney pedicle can be tied, or the kidney destroyed by traumatization, or the animal can be exposed during the registration to a severe bleeding which consequently causes a decrease of blood pressure and the amount of blood circulating through the kidney.

Goodman and Gilman[2] discuss the phenomenon of antidiuresis as follows:

a. Antidiuretics are automatically all drugs which decrease the blood pressure.

b. The neurohypophysis or, according to other authors, the hypothalamus, produces an antidiuretic hormone, the excretion of which is increased by various drugs, such as morphine, nicotine, and some of the barbiturates.

c. The antidiuresis increases the reabsorption of water from the provisional urine; it works on the proximal and distal tubuli contorti.

As it was explained above, when the differentiation of the ENG from the respiratory curves was discussed, the increase in diuresis is expressed by higher amplitudes of the curves until the acme of amplitudes is reached. Contrariwise antidiuretic measures show a decrease in amplitudes.

What does, therefore, the ENG express?

The ENG is the graphic demonstration of diuresis. The various physiological and pathological conditions which influence the diuresis seem to be well expressed by the changing curves.

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[2] Goodman, L. S. and Gilman, A.: The Pharmacological Basis of Therapeutics. New York: The Macmillan Co., 1955.

Without going into details concerning the shape of the curves, their amplitudes and frequencies, the curves seem to be not periodic and rather irregular. However, their mathematical as well as biological evaluation is easily possible and will be reported in another communication. Figure 3 shows a typical ENG together with the electroureterogram, the electrocardiogram, and pneumogram taken simultaneously from the same rabbit; pneumogram and electrocardiogram are registered on the same channel.

SUMMARY

The kidney produces electrical potentials which can be registered.

The renal curves can be unmistakably differentiated from the electrocardiogram as well as from the pneumogram. However, the renal potentials can be easily mistaken for the latter.

The renal potentials are different from the ureteral potentials.

The curves change according to whether the kidney is sandwiched between electrodes or needles are used. Furthermore, the position of the electrodes on the kidney is of some importance.

Each anatomical part of the kidney writes partial electrical potentials of its own.

Changes in the curves occur through diuresis and when antidiuretic measures are applied.

If the potentials of both kidneys are registered simultaneously, one kidney is always more active than the other and its tracings show higher amplitudes.

All investigations in this report were done on the rabbit kidney.

The importance of the ENG for renal physiology cannot be denied, since diuresis was confirmed graphically by the ENG.

How the ENG changes under pathological conditions shall be described in another communication.

The author wishes to record his deep gratitude to Dr. A. A. Luisada for his aid and constant encouragement.

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

CYSTITIS EMPHYSEMATOSA: CASE REPORT

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Cystitis emphysematosa is the presence of gas within the wall of the urinary bladder associated with inflammation. It was first described by Eisenlohr in 1888. Since that time approximately 30 additional cases have been found at autopsy. Ravich and Katzen reported the first authentic case in a living patient in 1932. They were obliged to perform suprapubic cystotomy to control hemorrhage from the bladder and thus made the diagnosis. This represents one of the most severe cases yet encountered. Antoine first observed this lesion through the cystoscope in 1934. In that same year Redewill made oxygen cystograms in one of his cases, but it was Lund in 1939 who first presented the typical appearance of cystitis emphysematosa on the plain x-ray. Twenty-two cases have been found during life, and the following is presented as the twenty-third case. It represents the fourteenth case in which the x-ray appearance has been described.

The patient was a 61-year-old man, a chronic alcoholic. He was admitted to the hospital on Christmas Eve 1954, having had increasing pain in the lower abdomen of about five days' duration. He had vomited once on the day of admission and had had poor appetite for 2 days. Nocturia and slowness of the urinary stream had been present for about two years. There was no exacerbation in these symptoms, and there was no dysuria or hematuria at the time of admission. His temperature was 99.2 and blood pressure was 130/80. There was moderate tenderness and definite muscle spasm in the lower abdomen especially on the right side. The prostate was found to be a small, firm gland on rectal examination. The white blood count was 17,000 with 84 per cent neutrophils. The clinical signs suggested appendicitis, but since the urine was reported loaded with pus cells, the patient was given gantrisin gm. 1 every 6 hours and was observed overnight. There was no glucosuria. The next day the temperature had returned to normal and most of the abdominal pain and tenderness had subsided.

On December 6, an x-ray of the abdomen was obtained, and it showed the distinctive findings of cystitis emphysematosa (fig. 1, *A*). It was noted that there was a collection of gas in the region of the urinary bladder and that it formed the usual shape of the bladder. One could see that this was not a single pocket of gas as might be present in the rectum. Rather it was divided into numerous tiny compartments indicating that it was present within the wall of the bladder. The small horns on each side probably were due to gas in the tissues about the lower ureters. In some of the previous reports a radiolucent ring in the bladder region has been described as the diagnostic feature of cystitis emphysematosa.

Accepted for publication July 21, 1955.
Read at annual meeting, Mid Atlantic Section, American Urological Association, Atlantic City, N. J. April 14–16, 1955.

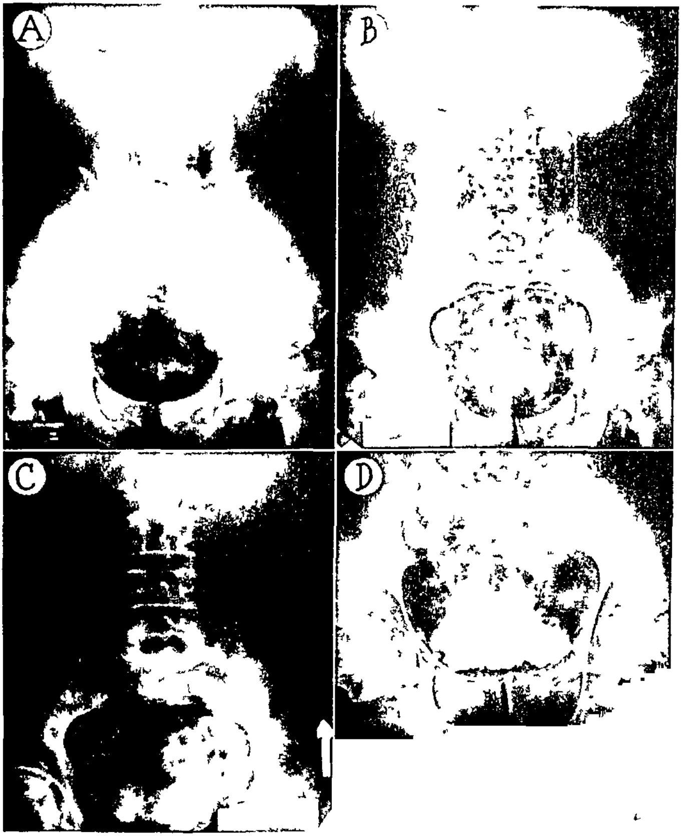

FIG 1 *A*, plain x ray of abdomen taken 7 days after onset of illness Emphysema of bladder wall clearly demonstrated *B*, excretory urogram 1 day later showing normal upper urinary tract and emphysema still present in distended urinary bladder *C*, upright film of excretory urogram showing fluid level in bladder with gas above *D*, cystogram taken 9 days after onset of illness showing large negative shadows resulting from large gas filled blebs in bladder wall

The following day excretory urography showed a normal upper urinary tract (fig 1, *B*) The gas was still present in the wall of the bladder, and in the upright position (fig 1, *C*) a fluid level was seen which indicated the presence of free gas within the bladder On the fourth hospital day a cystoscopic examination was made The urine was clear in appearance There was heavy trabeculation of the bladder wall, the result of a contracture of the bladder neck Scattered over

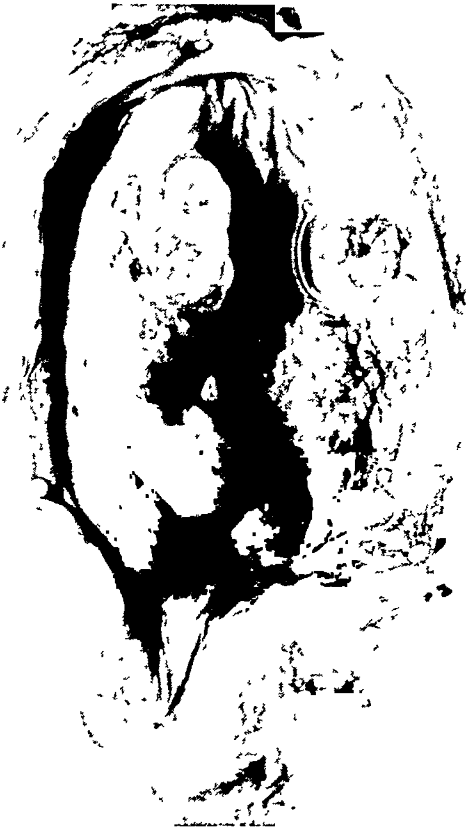

FIG. 2. Gross appearance of cystitis emphysematosa. Taken from case of Dr. Walter Putschar, Charleston, W. Va (Handbuch, von Henke-Lubarsch.)

the fundus of the bladder were numerous small vesicles. These varied in size up to at least 1 cm. in diameter and tended to be arranged in several groups. In a few places over the vesicles the mucosa was hemorrhagic, but there was not generalized severe cystitis. Two specimens were taken from the surface of the largest vesicles using the biopsy forceps. Figure 2 is taken from Dr. W. Putschar's case of 1934 and demonstrates the gross appearance of cystitis emphysematosa. The vesicles can be seen clearly, and the large ones have a glistening, almost translucent appearance so typical of emphysema. In our case the vesicles were not so thin walled and appeared similar to cystitis cystica. Others have reported that the vesicles had a silvery sheen from the reflected light of the cystoscope and would easily burst when touched with an instrument, but this was not true in our case.

Following cystoscopy a cystogram was made (fig. 1, *D*). The bladder outline was irregular due to the heavy trabeculations and the presence of gas within its walls. Several ovoid negative shadows were produced by the largest vesicles. The colon bacillus was cultured from the urine. Anaerobic cultures were negative. The biopsies showed an intact epithelium and submucosal tissue with only a slight sprinkling of chronic inflammatory cells.

The patient was discharged the next day and was given gantrisin for seven additional days.

He was next seen 2½ months later, and he stated that his urinary stream was stronger and there was less nocturia. A low grade B. coli urinary infection had persisted, and there were 3 ounces of residual urine. A glucose tolerance test was normal. Cystoscopy and cystography demonstrated that the emphysema had completely subsided. The disease in this case, as in most of the reported cases, was mild and of short duration.

DISCUSSION

Cystitis emphysematosa can be considered a pathological and clinical entity. The gas formation is a local manifestation involving the wall of the urinary bladder. Usually the gas will be present in the loose submucosal tissue and especially in the distensible portions of the bladder. Evidence of inflammation has always been found in the cases undergoing histological examination, and all the clinical cases have had urinary infection. The colon bacillus has been the most common organism found. In 3 cases Clostridium welchii was found, and it is interesting that two of these had a mild clinical course with few systemic manifestations. The third ran a febrile course and died a month later of streptococcic septicemia. Another constant feature is the presence of hemorrhage in the bladder wall. The clinical course varies in severity and behaves in similar fashion to B. coli urinary infections without emphysema. In all cases which were followed the emphysema was of short duration. In 11 of the 23 clinical cases the infection also subsided promptly, and the patient apparently had no further trouble. The remaining 12 patients had other lesions in the urinary tract such as chronic pyelonephritis, hydronephrosis, and chronic urinary retention. The course in these associated diseases did not seem to be altered by the brief appearance of the cystitis emphysematosa.

Redewill in 1934 attempted to subdivide cystitis emphysematosa into several distinct types, and several authors since have adopted his classification:

Group 1: Fulminating cases of generalized sepsis due to a gas bacillus with bladder involvement.

Group 2: Cystitis emphysematosa with a colon bacillus infection.

Group 3: Cystitis emphysematosa found in diabetics without urinary infection.

Group 4: Cystitis pneumatosis cystica in which the air was thought to be collected into true cysts lined by endothelium. The trauma of instrumentation was believed to be a factor in this group but infection played no role.

With the accumulating data from the case reports the need for this classification seems questionable. The first group probably should be considered a systemic disease and not a form of cystitis emphysematosa. The second group is the entity being discussed in this paper and should be expanded to include any bacteria even local infections with Clostridium welchii, as in Antoine's, and in Levin's cases. Since infection has proven to be a constant finding in the clinical cases, there is no reason to consider group 3 or 4 apart from the second group. The cysts lined by endothelium are generally interpreted to be distended lymphatics and not true cysts. The transient nature of the emphysema would also make true cyst formation improbable.

The etiology is still uncertain. The most probable explanation is that bacterial enzymes act on tissue fluids to produce the gas. Twelve of the 23 patients have had diabetes mellitis and perhaps the increased concentration of glucose in the interstitial fluids may predispose to gas formation. Our case is the only one reported in a chronic alcoholic.

SUMMARY

The twenty-third case of cystitis emphysematosa in a living patient is presented together with x-ray and cystoscopic description. Cystitis emphysematosa is considered a clinical and pathological entity.

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* Arranged chronologically.

The Journal of Urology
Vol 75 No 2 February 1956
Printed in U S A

THE MANAGEMENT OF HUNNER'S ULCER BY DIFFERENTIAL SACRAL NEUROTOMY PRELIMINARY REPORT

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Intractable pain and frequency are the most incapacitating features of Hunner's ulcer and of chronic interstitial cystitis [1, 2] In an effort to reduce bladder hypertonicity and to increase bladder capacity, differential sacral neurotomy has been done in two such cases after blockage of S 3 bilaterally with 1 per cent xylocaine indicated a beneficial effect of this procedure

Reduction of the parasympathetic outflow to the detrusor and of the sacral somatic outflow results in increased bladder capacity, as has been demonstrated by the effect of differential sacral neurotomy in the management of the neurogenic bladder [3-8] The use of sacral neurotomy in instances of interstitial cystitis and of Hunner's ulcer, at best, is still in an experimental stage The degree of fibrosis of the bladder wall seems to be the determining factor in the use of sacral neurotomy An increase in bladder capacity by reduction of the sacral somatic outflow can only be attained as long as the elasticity of the bladder wall is still preserved The extent of differential sacral neurotomy can best be determined on the basis of preoperative diagnostic sacral block studies

In one case of chronic interstitial cystitis (N-79), fibrosis of the bladder wall was so far advanced that neither spinal anesthesia nor sacral block studies resulted in an increase in bladder capacity Sacral neurotomy was not considered in this case In case 2 (N-173), bilateral section of S 3 resulted in an increase of bladder capacity from 40–80 cc to 600 cc, relief of pain and normal micturition In case 3 (N-131), bilateral neurotomy of S 3 brought about an increase in capacity from 50–80 cc to 180–300 cc, relief of pain and reduction of frequency It is possible that additional section of S-2 bilaterally may still improve the result in this case

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Accepted for publication September 21, 1955

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ILLUSTRATIVE CASE

A 31-year-old white, married woman (N-173) had suffered from chronic interstitial cystitis, marked frequency and intractable pain for a period of 5 years. During the past year, she had been unable to engage in any social activities because of the ever-increasing frequency, accompanied by intractable pain. At day and night, she was unable to hold her urine longer than 45 minutes to 1½ hours. Blocking of the S-3 root bilaterally with 1 per cent procaine on June 7, 1954, resulted in a capacity of 180 cc. The patient was relieved of all pain and was able to empty her bladder without residual and without incontinence. Pain and frequency recurred 36 hours after the block. On June 11, 1954, the S-3 block was repeated and a similar result obtained. Sacral neurotomy of S-3 was performed on June 15, 1954. Immediately following operation, the patient was able to void without straining, without residual and without incontinence. Her bladder capacity was 600 cc and she had no bladder pain. During a 12-month followup period, the patient's condition remained that of the immediate postoperative status. She has had no return of pain or frequency. The bladder capacity has remained 600 cc.

DISCUSSION

Reduction of bladder hypertonicity and increase of bladder capacity appear to reduce or alleviate the distressing symptomatology of Hunner's ulcer and chronic interstitial cystitis. Dr. D. K. Rose, in a personal communication, suggested that elimination of impulses carried by the third sacral roots serves to reduce hyperirritability of the urethra-bladder reflex. Experience with the employment of sacral neurotomy in the management of the neurogenic bladder suggests that reduction of muscle tone in the bladder wall and resulting increase in bladder capacity are additional factors in the relief of pain and dysuria.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

RADIOGRAPHIC ESTIMATION OF RESIDUAL URINE IN CHILDREN

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Residual urine, as one indication of early detrusor decompensation, is a valuable clinical sign.[1] As a diagnostic procedure, it is perhaps comparable to the elevated venous pressure or basilar rales as signs of cardiac failure. In adults, it constitutes mainly corroborative evidence and is rarely used alone as an indication of vesical neck obstruction, except in neurogenic dysfunction of the bladder.

Howard and Buchtel[2] have reported the instillation of mineral oil into the bladder as a method for determination of residual urine in children. Mineral oil floats by virtue of its specific gravity of less than 1.000, and will be partially retained in the bladder if there is any residue present. If oil is obtained by catheterization 24 hours after its instillation, this then can be taken as evidence of residual urine. This is in consonance with the common experience of floating paraffin particles, persistent cod liver oil or oily medications remaining in the bladder for months at a time in the partially decompensated bladders of elderly patients. Howard and Buchtel's mineral oil technique has been quite generally used and reliable results have been obtained with this method.[3] Moreover, in children, it may frequently be the most reliable sign of vesical neck obstruction in need of surgical relief. The substitution of a radiopaque material for mineral oil permits serial roentgenographic recording of residual urine over a period of days without repeated catheterization. For this purpose, we have employed 10 per cent "ascendent" lipiodol.

METHODS AND MATERIAL

Ascendent lipiodol 10 per cent* is supplied in 5 cc. ampules by the manufacturer and the entire contents are instilled into the bladder with a catheter. This is frequently carried out at the close of cystoscopic study. A film of the abdomen is then made. If the patient is under anesthesia, no further films are taken and the patient is returned to bed. During the next 24 hours, the patient is permitted to void at will and a delayed film is then exposed (fig. 1). If remaining oil is noted, a 48 hour film is obtained. Further films can be taken at daily or weekly intervals as indicated. Both upright and supine films are made each time, the upright film frequently being the more revealing as the oil presents a thicker layer to the x-ray beam in this position. A film of the entire abdomen

Accepted for publication September 21, 1955.

[1] Kirwin, T. J. and Hawes, G. A.: The diagnostic value of residual urine estimation. J. Urol., 41: 413–430, 1939.

[2] Howard, T. Leon and Buchtel, H. A.: Resection of vesical neck in children. Indications and results. J.A.M.A., 146: 1202–1206, 1951.

[3] Buchtel, H. A.: Personal communication.

* The lipiodol used in this study was kindly supplied by E. Fougera and Co., 75 Varick St., New York 13, N. Y.

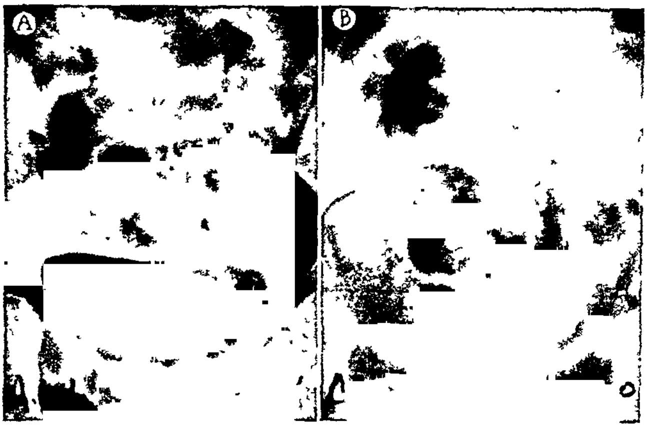

FIG. 1. Case 1. Children's Hospital, D16822, A. M. W., 2-year-old girl, was admitted following single episode of fever and pyuria which had responded promptly to antibiotics. Pyelograms were within normal limits. Cystoscopy disclosed adequate vesical neck and urethral caliber was approximately 16F. There was no trabeculation. Urine has remained uninfected.

A, film of bladder following instillation of 5 cc of ascendent lipiodol. There is also some remaining aqueous contrast medium in bladder. Instillation was performed at close of a pyelographic study.

B, 24-hour film to show complete evacuation of ascendent lipiodol confirming absence of residual urine.

to include the renal area is important, since reflux of the oil to the kidney pelvis can be demonstrated in occasional cases. This finding may be of great value in explaining the pathogenesis of pyelonephritis in a given case.[4-7]

Lipiodol is a compound of iodine and poppy seed oil; its standard form contains 40 per cent iodine by weight. Ascendent lipiodol, though containing less iodine by weight (i.e., 11 centigrams/cubic centimeters as contrasted with "heavy" containing 54 centigrams/cubic centimeters), is adequately opaque for radiological purposes. It has been proven relatively nontoxic and has been well tolerated when introduced into many body cavities.

The test for residual urine was carried out in 20 children and two adult males, all of whom had been referred for urological study. There were 15 girls and 5 boys. The children's ages ranged from 6 weeks to 11 years. There were no untoward reactions and no evidence of urethral or vesical irritability due to the drug.

RESULTS

Nine patients showed retention of the light lipiodol for 24 hours or longer and the remaining eleven showed no evidence of radiopaque oil on the 24-hour film (figs. 2–7).

Studies comparing the behavior of light and heavy lipiodol in the bladder were made in a 65-year-old man who was admitted for urological diagnosis following the discovery of gross pyuria (figs. 8–10).

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[4] Stewart, C. M.: Delayed cystograms. J. Urol., 70: 588–593, 1953.

[5] Bunge, R. G.: Delayed cystograms in children. J. Urol., 70: 729–732, 1953.

[6] Bunge, R. G.: Further observations with delayed cystograms. J. Urol., 71: 427–434, 1954.

[7] Sicard, Jean Athanase and Forestier, Jacques: The Use of Lipiodol in Diagnosis and Treatment. A Clinical and Radiologic Survey, Oxford University Press, H. Milford, 1923.

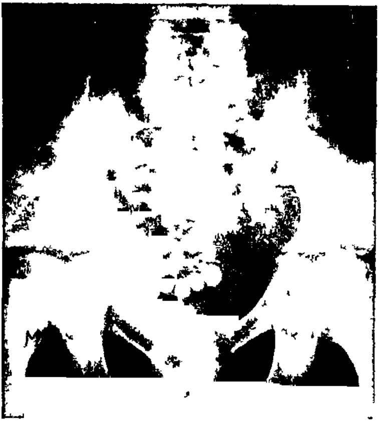

Fig 2 Case 2 SUH E21825, M K, an 11 year old boy, had been followed since age of 3½ with urinary and fecal incontinence secondary to epidural cyst of neural canal Following excision of cyst at the age of seven, he voided well with no residual, but subsequently overflow incontinence, pyuria, progressive hydroureter and hydronephrosis developed and, following finding of residual urine of 300 cc had retropubic wedge resection of vesical neck Postoperatively he continued to have residual urine of 20 cc and was forced to strain and aid his bladder evacuation with Credé maneuvers Cystoscopy showed mechanically adequate vesical neck, heavily trabeculated bladder and patulous left ureteral orifice

Globules of ascendent lipiodol remain in bladder on immediate post voiding film

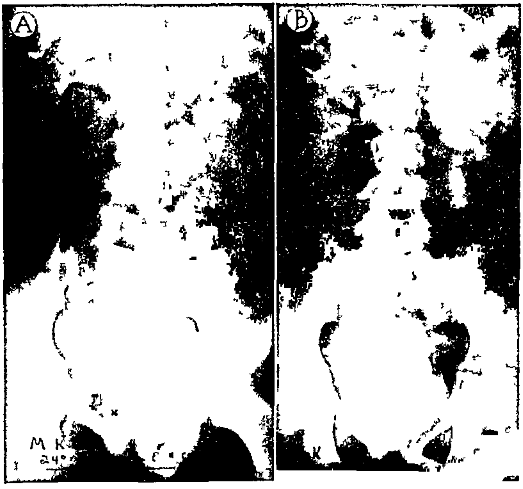

Fig 3 Case 2 *A*, remaining oil droplets in bladder and reflux of oil to left kidney at 24 hours indicating residual urine and incompetent left ureterovesical valve mechanism

B, cystogram with aqueous contrast medium confirming left renal reflux Oil in hydronephrotic renal pelvis can be seen as rounded shadows of increased density within pyelogram

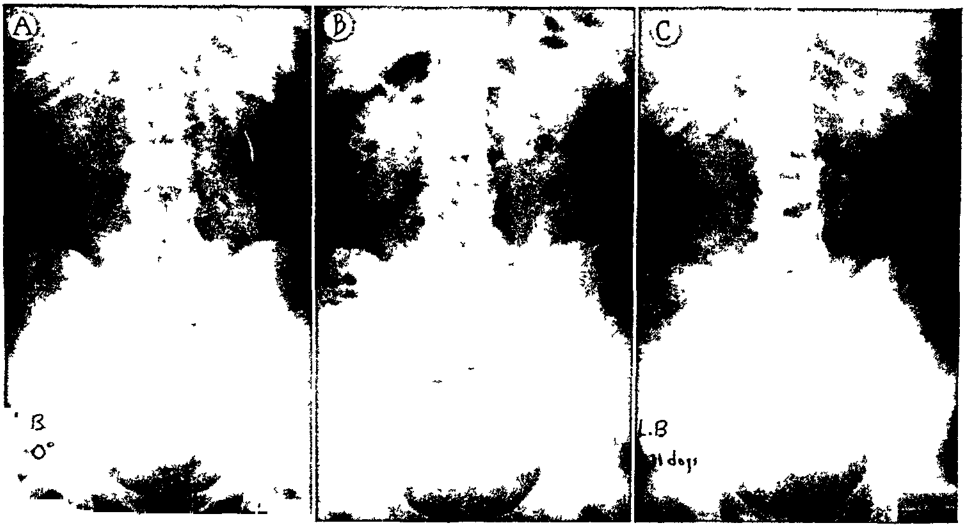

FIG. 4. Case 7. SUH 339532, L. B., 11-year old girl, had a history of recurrent urinary tract infection since the age of 5 months. Urological studies had revealed bilateral hydronephrosis and hydroureters at age of two and large residual urine was noted. Diagnosis of vesical neck obstruction was established, requiring two transurethral resections of vesical neck at the ages of 3 and 4 years. Following these procedures her residual urine was found to vary between 60 cc and 240 cc. Cystoscopy disclosed apparently open vesical neck with no evidence of urethral obstruction. Bladder was heavily trabeculated and single small diverticulum was noted behind left ureteral orifice. Residual urine varied between 10 cc and 125 cc. There was grade 1 hydroureteronephrosis bilaterally.

A, upright film of abdomen following instillation of ascendent radiopaque oil.

B, remaining oil at 48 hours. Reflux to left kidney has occurred and several flecks of medium can be seen in calyceal system.

C, remaining oil in left renal pelvis and bladder at 11 days.

A second adult was a 62-year-old man who had had perineal prostatectomy 1 year previously for a large, benign adenoma and, though he had no residual urine or pyuria, continued to have symptoms of urgency and frequency and a small urinary stream. He was found by cystoscopy to have a contracture of the vesical neck and was undergoing a series of Kollman dilatations of the vesical neck to which he was responding satisfactorily. Five cubic centimeters of light lipiodol were instilled and a 24-hour film showed the oil to be absent, confirming the fact that he was able to evacuate the bladder completely.

Decompensation of the detrusor based on vesical neck or subvesical obstruction of a mechanical, neurogenic or inflammatory nature was present in all of the children who showed retention of the light lipiodol for 24 hours or longer (table 1) and in the single adult with the prolapsed bladder base. In the remaining children and one adult who were able to evacuate the bladder completely in 24 hours, there was no decompensation of the detrusor mechanism. Reflux of the oil to the kidney occurred in 3 patients, all of whom had residual urine. In these cases, despite the fact that two had hydronephrosis, it was found that the refluxed oil disappeared from the kidney in from 7 to 11 days with no particular measures other than the patients' normal activity. It was anticipated that it might then be necessary to place the patients in the knee-chest position or to have them sleep in the Trendelenburg position, but this was not necessary.

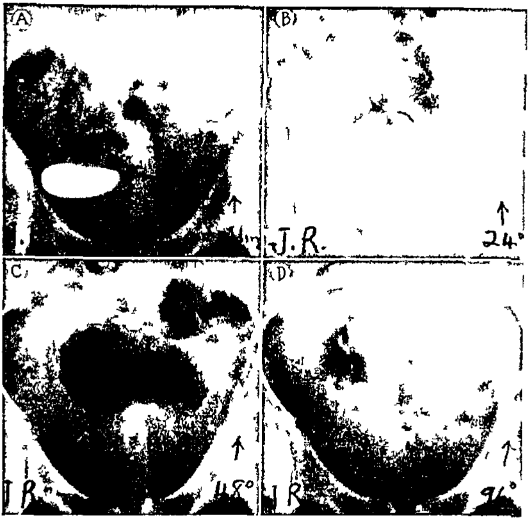

FIG. 5. Case 9. Children's Hospital D16359. J. R., 11 year old girl with 3 year history of recurrent urinary tract infection without fever was admitted for urological study following recurrence due to E. coli. Excretory urograms showed normal upper urinary tract. Cystoscopy disclosed urethra which was snug to the 18F sheath. There was some edema and a few polyps were found at vesical neck. Caliber of vesical neck was adequate. There was no trabeculation. Ureteral orifices were questionably enlarged but not patulous. Urine sediment was loaded with leukocytes and bacilli which were identified as E. coli. Measured residual was 8 cc. Infection responded to antibacterial therapy and 3 months later there had been no recurrence.

A, appearance of floating radiopaque oil immediately post voiding.

B, remaining oil at 24 hours in vertex of bladder.

C, remaining oil at 48 hours with patient in upright position. Oil presents thicker layer to x ray beam in this view as contrasted with supine position in which it floats against interior wall of bladder.

D, absence of oil at 96 hours. Diagnosis in this case is still obscure. Internal sphincter spasm secondary to acute cystitis is most probable explanation for delayed emptying.

Apparently ureteral peristalsis was sufficient to propel the oil droplets into the bladder.

DISCUSSION

In the adult the test for residual urine is simple and the measurement remarkably reproducible. The patient is instructed to urinate, emptying the bladder as completely as possible, following which catheterization is carried out and the remaining urine measured. This procedure is as accurate as necessary for the value it adds to the diagnosis.

Radiographically, a rough estimate of residual urine in adults can be obtained during the course of intravenous urography if a post-voiding film of the bladder is taken at the end of the examination. The presence of residual urine has more

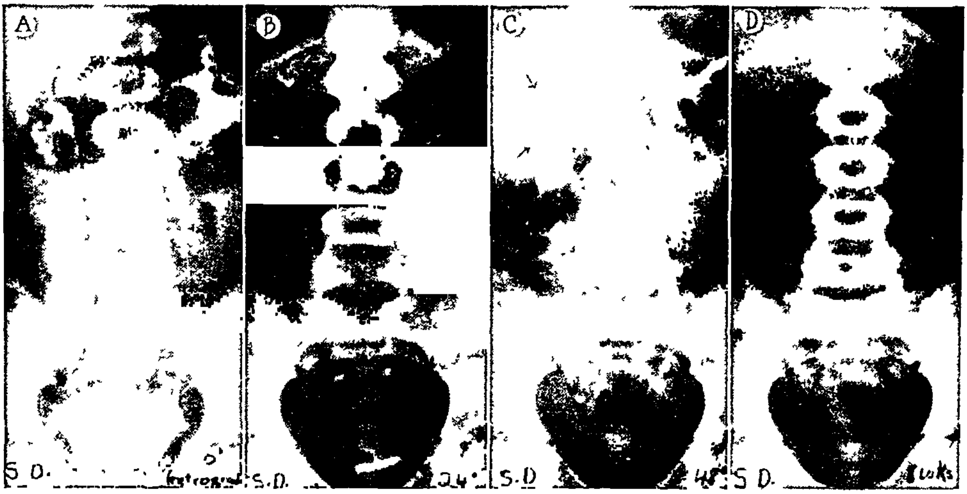

Fig. 6. Case 10. Children's Hospital, D15304, S. D., a 4-year-old girl, was admitted for urological study with history of recurrent urinary tract infection with fever of 4 months' duration. Predominant organisms in past had been E. coli and Staphylococcus albus, and infection had responded partially to antibiotics. On admission, urine contained 6 to 10 leukocytes per high power field and E. coli were obtained on culture. Pyelography disclosed evidence of calyceal scarring or spasm in right kidney and multiple deformities of right ureter interpreted as ureteritis. Cystoscopy showed apparently normal vesical neck. However, bladder showed 2 plus trabeculation. Ureteral orifices were normal in size, shape and position. Measured residual of 15 cc was obtained. Diagnosis of vesical neck obstruction was made and retropubic wedge excision advised.

A, retrograde pyelogram.

B, remaining ascendent lipiodol in bladder at 24 hours. Reflux of oil can be seen in right kidney. Pathogenesis of right pyelonephritis could not be more apparent.

C, 48-hour film showing persistence of oil droplets in bladder and right kidney.

D, film of abdomen taken at 8 weeks reveals all of contrast medium to be absent. Bladder catheterization had been carried out in interim, but no attempt was made to aid evacuation of oil in right kidney. Peristalsis and positional changes with patient's normal activity were apparently adequate to complete its evacuation.

diagnostic importance in children and yet, perversely enough, is more difficult to determine. The diagnosis of vesical neck obstruction can be difficult, for cystoscopic observation of the vesical neck in children can be very misleading. The appearance of the vesical neck varies with the degree of distention of the bladder. In some cases the alteration of caliber is only a matter of millimeters and often a brief impression has to suffice for a diagnosis. Trabeculation of the bladder in its more minor degrees can be easily confused with normal muscle striations which appear beneath the mucosa at extremes of distention or under the sudden stimulus of an involuntary detrusor contraction. Patulous ureteral orifices may mean vesical neck obstruction or primary ureteral disease. The demonstration of persistent residual urine is frequently of vital importance in reaching a decision as to the presence or absence of obstruction at the vesical neck.

The obstacles to accurate residual urine determination in children are two: 1) inability of the child or infant to void on command due to strange office or hospital surroundings, emotional patterns or non-comprehension; 2) doubt by the physician as to whether the child has voided as completely as possible; 3)

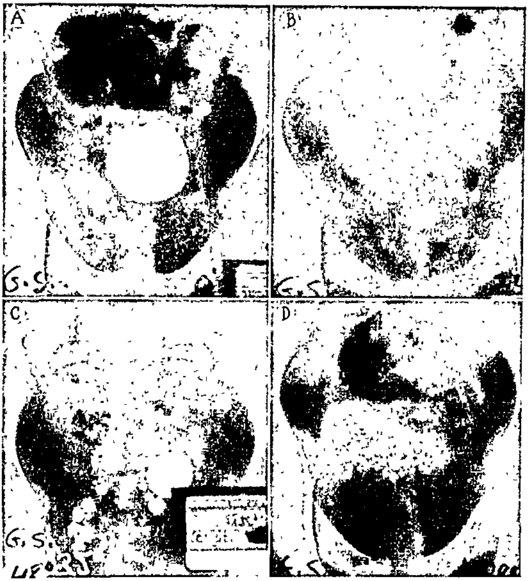

Fig. 7 Case 13 SUH, 335292, G. S., a 5-year-old girl with a 2-year history of recurrent pyuria unassociated with fever, was admitted for restudy following inability to control infection with all antibiotics Predominant organisms had been E. coli and B. proteus. Excretory urograms showed normal upper tracts bilaterally Measured residual urine of 6 cc was obtained. Cystoscopy disclosed questionable vesical neck contracture, but 2 plus trabeculated bladder.

A, initial film following instillation of ascendent lipiodol

B, film made at 24 hours to show persistence of medium.

C, remaining oil at 48 hours. There has been some dispersion of droplets.

D, film made at 1 week to show persistence of contrast medium. Wedge resection of vesical neck was subsequently carried out following which it became possible for first time to sterilize bladder urine.

an additional consideration is the emotional trauma associated with catheterization of the small child.

The actual volume of residual urine is not as important as whether or not it is persistent. It is not paramount to know how badly the detrusor mechanism is decompensated. The fact that it is decompensated at all is the significant point. Ascendent lipiodol instillation, though requiring catheterization, has the advantage of requiring only a single procedure of this type, subsequent information being obtained and documented radiographically. The physician can feel a definite security if all of the lipiodol is absent at the end of 24 hours. In some children an immediate post-voiding film will show absence of the oil, in which case the study is complete. However, it is desirable to allow a child to engage in

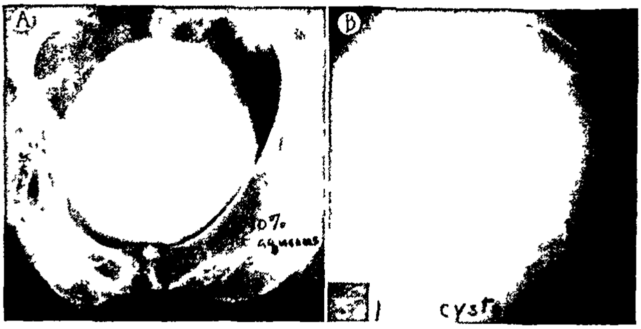

FIG. 8. *A*, anteroposterior view of cystogram of 65-year-old man 1 year following abdominoperineal resection of rectum for carcinoma. Trabeculation was secondary to adenoma of prostate which had been enucleated 5 years previously.

B, lateral view of cystogram to show base of bladder lying in hollow of sacrum. Base of bladder was actually below level of vesical neck with patient standing.

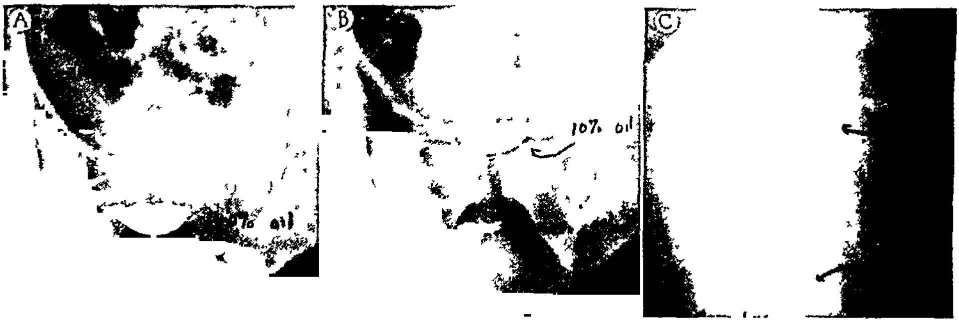

FIG. 9 *A*, anteroposterior view of bladder containing 40 per cent (heavy) lipiodol and small volume of sterile water Rounded inferior surface of globule represents oil lying on posteriorly prolapsed bladder base.

B, post-voiding film of bladder containing 5 cc of light lipiodol, 150 cc of sterile water and small amount of remaining heavy lipiodol. Major portion of dependent lipiodol was evacuated with initial urine upon micturition

C, lateral post-voiding film to show remaining collections of heavy lipiodol in bladder base and at vesical neck. Ascendent lipiodol floats on dome of bladder.

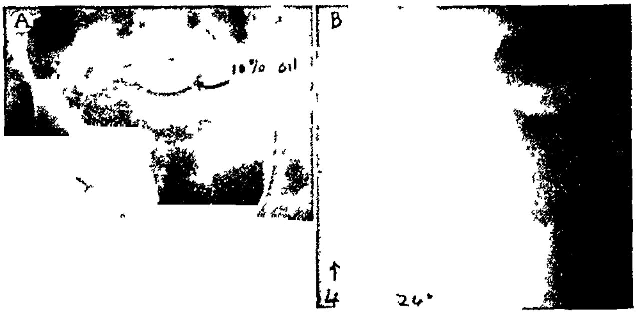

FIG. 10. *A*, film made at 24 hours to show remaining ascendent lipiodol, but complete absence of heavy oil

B, lateral view to show absence of heavy lipiodol in bas-fond but persistence of light lipiodol in vertex. Patient had residual urine of 125 cc, as measured by catheter on several occasions.

several leisurely urinations over a 24-hour period without the pressure of being commanded to void on the spot.

One facet of the problem of vesical neck obstruction that needs further study is the concept of spasm of the internal sphincter. It is well known that urethral

TABLE 1 *Correlation of cystoscopic findings and diagnosis with presence or absence of persistent residual urine as assessed by ascendent lipiodol instillation*

Case	Cystoscopy Vesical Neck	Trabeculation	Residual	10% Ascendent Lipiodol		Diagnosis
				Absent	Present	
1 H P F 11 yrs	negative	minimal	?	24 hrs	—	Pyelonephritis
2 M K M 11 yrs	negative	marked	20 cc	—	72 hrs +	Neurogenic bladder postoperative wedge resection
3 C H F 5 yrs	negative	none-minimal	30 210 cc	24 hrs	—	Bilateral congenital ureterovesical juncture obstruction
4 M H F 3 mos	negative ?	none	?	24 hrs	—	Cystitis
5 M P F 6 wks	negative ?	minimal	?	24 hrs	—	Cystitis
6 L A F 2 yrs	negative	none	?	24 hrs	—	Pyelonephritis
7 I B F 11 yrs	negative ?	marked	10 125 cc	—	11 dys +	Congenital contracture vesical neck
8 A M W F 2 yrs	negative	none	?	24 hrs	—	Pyelonephritis
9 J R F 11 yrs	negative ?	none	8 cc	—	48 hrs	Cystitis urethritis severe
10 S D F 4 yrs	negative ?	moderate	15 cc	—	48 hrs +	Congenital contracture vesical neck
11 A R F 6 yrs	negative	none	?	24 hrs	—	Pyelonephritis
12 D G M 10 yrs	negative	minimal	5 cc	—	48 hrs	Neurogenic bladder
13 G S *F 5 yrs*	*contracture*	*moderate*	*6 cc*	—	*7 days*	*Congenital contracture vesical neck*
14 P B F 11 yrs	negative	none-minimal	15-200 cc	—	48 hrs +	Neurogenic bladder
15 P R M 6 yrs	negative	none	?	24 hrs	—	Purpura bladder
16 A McC M 5 yrs	negative	none	?	24 hrs	—	Meatal stenosis
17 K H F 1½ yrs	negative	none	?	24 hrs	—	Bacilluria ? etiology
18 S W F 4 yrs	negative	none	?	—	72 hrs	*Urachal cyst, cystitis severe*
19 R C F 3 mos	negative	none	?	24 hrs	—	No disease
20 J C M 1½ yrs	negative	moderate	5 cc	—	72 hrs	Congenital contracture vesical neck Postoperative wedge resection

dilatation sometimes effects dramatic relief from episodes of recurrent urinary tract infection in female children. Occasionally one or two urethral dilatations will cause a marked improvement. The commonly held views are that a urethral stricture is being dilated or that a mucosal flap has been ruptured. Some feel that the psychological trauma of a urethral dilatation alone is responsible. It seems more probable, however, that it is smooth muscle spasm at the internal sphincter that is being treated by over dilatation. In two of our cases (J. R., case 9 and S. W., case 18) there were insufficient findings to establish definitely the diagnosis of mechanical or neurogenic obstruction and yet the lipiodol was retained for over 72 hours. The study had been performed in these cases just as acute cystitis was subsiding and there were still inflammatory changes in the region of the vesical neck and trigone. Subsequent lipiodol studies made in one of these patients during a quiescent phase demonstrated complete emptying at 24 hours. A word of caution then is indicated in marginal cases where internal sphincter spasm may be responsible for some temporary retention. Urethral dilatation, antibiotics and antispasmodic medication should be instituted before wedge resection of the vesical neck is considered.

There appears to be very little danger associated with ascendent lipiodol studies of residual urine. Oil is certainly not an unknown substance in the urinary tract and has been used for many years by urologists for bladder instillations, diagnostic tests and lubrication of catheters.[8, 9] It may be unwise to instill any oil into the urinary bladder in the presence of active venous bleeding as might occur from the prostatic fossa because of the possibility of producing an oil embolus, unlikely though this may be. In this group of cases, bleeding has been considered the only contraindication to the performance of the study. Ordinary care in the avoidance of trauma to the mucosa of the urethra and bladder is of course important if oil embolus is to be avoided.

The possibility of a retained globule of oil forming the nidus of a calculus was considered and it would seem that this is a possibility if it were allowed to remain for an extended period or were trapped in a stenosed minor calyx following reflux from the bladder. It is our custom when the study has been completed to make a final film to be certain that all of the oil has been evacuated.

SUMMARY

An accurate radiographic method for establishing the presence of residual urine in children is presented in which 5 cc of ascendent lipiodol is instilled into the urinary bladder by catheter and its presence or absence determined by roentgenogram in 24 hours and at subsequent intervals if indicated.

The procedure was carried out in 20 children and 2 adults without untoward effect. Nine of the children and one adult showed retention of the radiopaque oil for 24 hours or longer and in all of these patients pathological lesions were found to be responsible for some degree of detrusor decompensation. The eleven children who were able to evacuate the oil in 24 hours showed no obstructive lesions. The remaining adult was found to have a compensated detrusor mechanism in the presence of a contracted vesical neck.

No untoward effects were encountered following this procedure.

490 Post St., San Francisco 2, Calif. (B. W. Y.)

[8] Neuswanger, C. H.: Iodized oil as a pyelographic medium. J.A.M.A., 84: 1816, 1925.

[9] Neuswanger, C. H.: Iodized oil as a pyelographic medium. Surg., Gynec. & Obst., 43: 169-176, 1926.

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

SOME STUDIES OF URINARY INCONTINENCE IN MEN

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The urinary sphincters and their actions are so poorly understood that ideal correction of severe post-prostatectomy incontinence is not often achieved. Definition of the structures involved and observations of their dynamics should add useful information.

PART 1: HISTOLOGICAL STUDIES

The limits and course of the external sphincter would seem determinable from a histological study of properly selected and prepared specimens. Specimens consisting of the bladder, prostate, membranous urethra, and much of the surrounding tissues were obtained from the fresh bodies of males seven, twelve, nineteen, and forty years of age. None had recognized urinary disorders before death. Each specimen was first cut into large blocks, and then multiple sections were cut in full cross section, stained with hematoxylin and eosin, and mounted for microscopic examination. Approximately every other section was stained with either Masson's trichrome stain or phosphotungstic acid and hematin stains.

Two sections were cut at approximately each millimeter, except for the specimen from the 12 year-old boy, which was divided more closely. The first preparations were made through the membranous urethra, and the later ones were numbered consecutively backwards towards the bladder. The puboprostatic ligaments, which play a not inconsequential role in urinary control, especially in women, were not included in this microscopic study.

Three hundred and forty consecutive sections were made in the three blocks of the specimen from the 12-year old boy (fig. 1). A complete ring of striped muscle was around the membranous urethra and continued around the prostate until the fifty-fourth section was reached. At this point, estimated to be between 1 and 1.5 cm. proximal to the prostatic apex, the ring was first interrupted in the basal or rectal side. However, the anterior sheath and lateral capsule of the prostate continued through the 120th section to be formed of this muscle. The fibers comprising this muscle coursed in various directions; they did not form a circular ring. Penetrations of this muscle went as deeply as two thirds of the distance to the urethra, and the glandular elements often rested directly on these deep extensions (fig. 2). The capsular muscular bundles appeared to have no constant directional pattern. After the eighth slide from block B this muscle was seen no more. Examination of the remaining preparations failed to reveal a grouping of circumferential smooth muscle fibers which could be designated a separate sphincter in the vesical outlet; in fact, there were about as many longitudinal bundles as circular. A rich plexus of nervous tissue hugged the base of the bladder and proximal portion of the prostate.

Read at annual meeting, American Urological Association, Los Angeles, Calif., May 16-19, 1955.

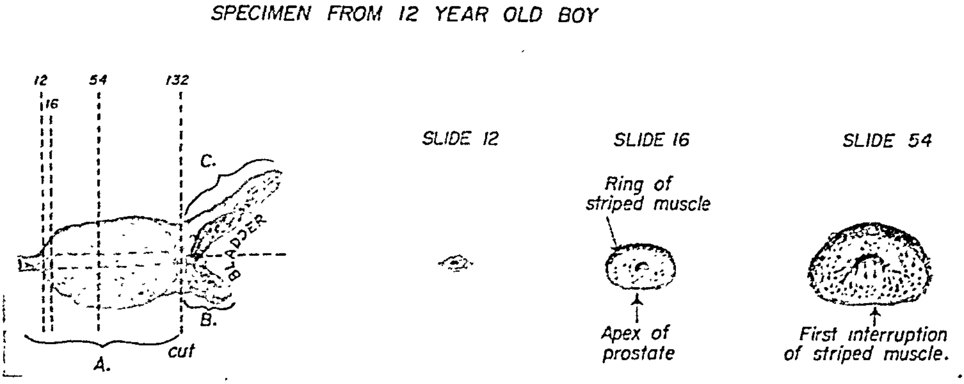

FIG. 1. Drawing of gross specimen and cross sections from 12-year-old boy.

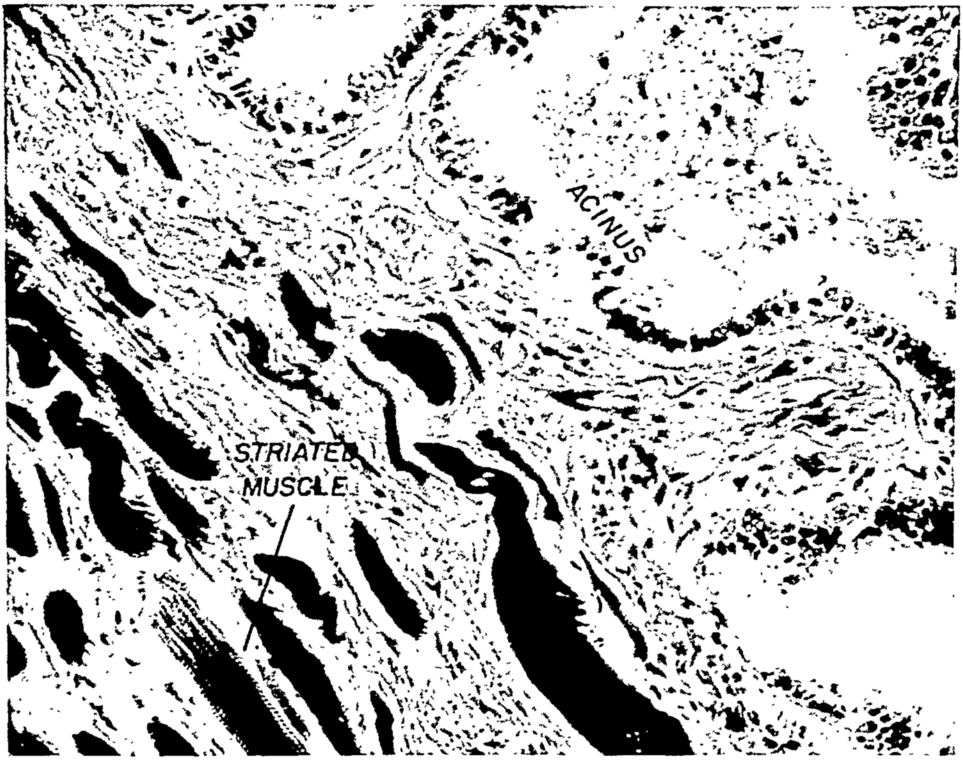

FIG. 2. Photomicrograph of cross section, using high magnification, showing glandular elements intimately associated with striated muscle.

Examination of the specimen from the 7-year-old boy revealed similar arrangements except that the striated muscle forming all of the dorsal portion of the prostatic capsule continued all the way from the membranous urethra to the vesical outlet (fig. 3). Near the prostatic apex (slide 18), thick downward extensions of the muscle penetrated the gland as if to seize the urethra like pincers (fig. 4). No clearly defined circular muscle was seen at the vesical outlet.

This same striated muscle was found about the membranous urethra and

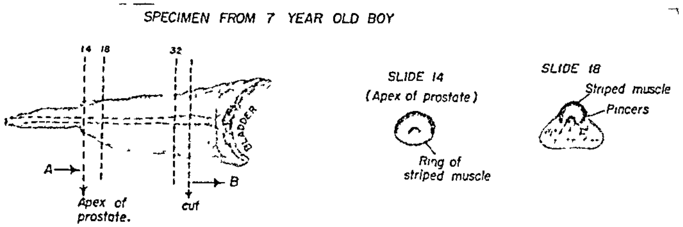

FIG 3. Drawing (over-elongated) of specimen and cross sections from 7-year-old boy.

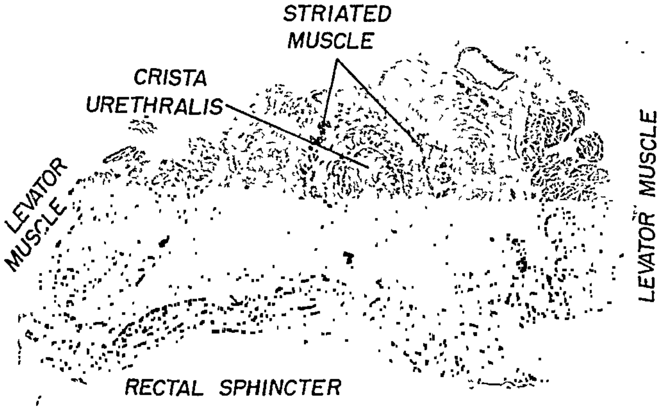

FIG. 4. Photomicrograph of cross section slightly less than one centimeter from prostatic apex of 7-year-old boy. Darkly stained striated muscle in peripheral, and especially lateral, portions of gland was prominent.

prostatic apex in the specimen from the nineteen-year-old boy (fig. 5). Striped muscle vanished in the basal portion of the capsule after slide 20 of the seventy made from block A (fig. 6). The anterior capsule continued to be completely made up of this muscle until the sixty-second section. Fragments remained through section 6 in the 92 from block B. Penetrations into the glandular substance were again noted. The vesical outlet was not suitably prepared for further studies.

The first sections of the ninety-four from the last specimen, that from the 40-year-old man (fig. 7), were at the prostatic apex. Here large bands of circular striped muscle were present in the peripheral prostate. At section 14, 7 mm. from the apex, only a heavy layer remained as the anterior capsule, and none was noted in the composition of the lateral portion of the capsule. At section

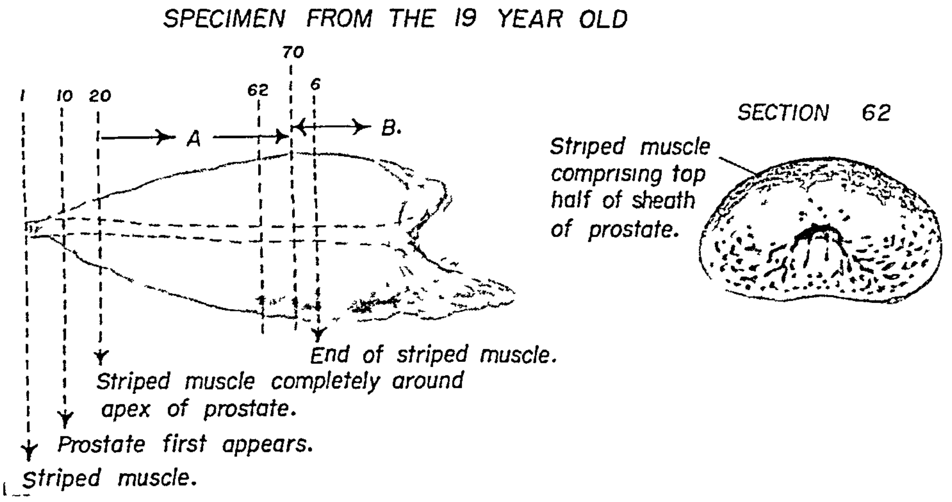
SPECIMEN FROM THE 19 YEAR OLD
70
1
10
20
62
6
A
B.
SECTION 62
Striped muscle comprising top half of sheath of prostate.
End of striped muscle.
Striped muscle completely around apex of prostate.
Prostate first appears.
Striped muscle.

FIG. 5. Drawing of specimen and cross section from 19-year-old boy.

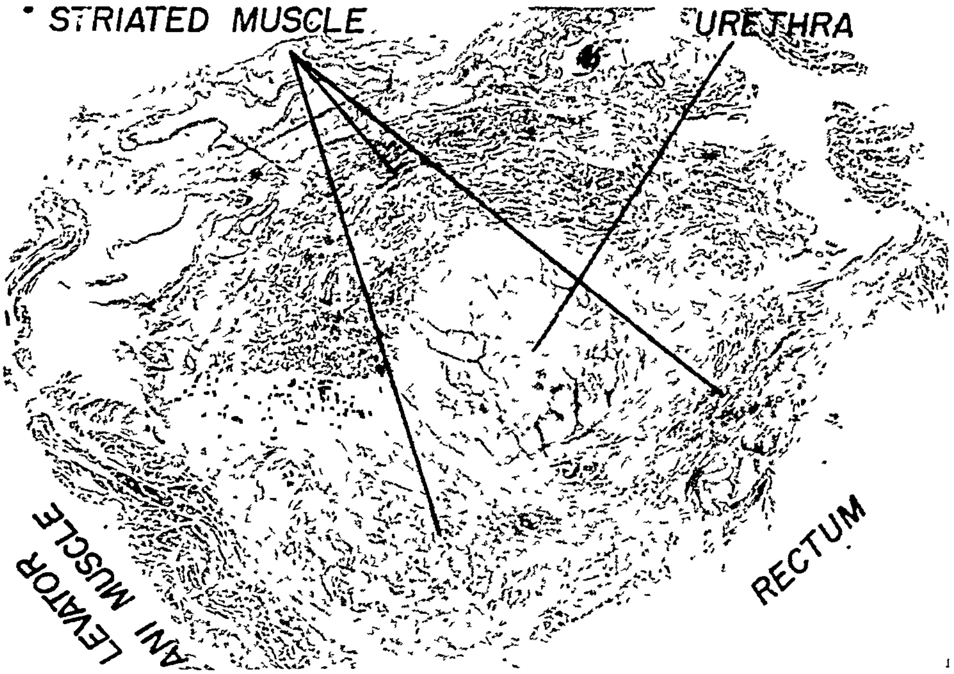

FIG. 6. Low power photomicrograph of cross section through prostatic apex of 19-year-old subject. Prostate is surrounded by striated muscle, thick dorsally but thin and fragmentary on rectal side

26, 1.3 cm. from the apex, trabeculae of striped muscle were especially noted in the gland. This muscle in the anterior capsule disappeared between sections 4 and 7 in block B (slightly less than 5 cm. from the prostatic apex).

Thus, in all four of these normal specimens a thick circular mass of striated muscle (external sphincter) was found around the membranous urethra *and* prostatic apex. In fact, this muscle formed the prostatic capsule in the apical portion, and in the dorsal aspect the muscle continued much farther. In the speci-

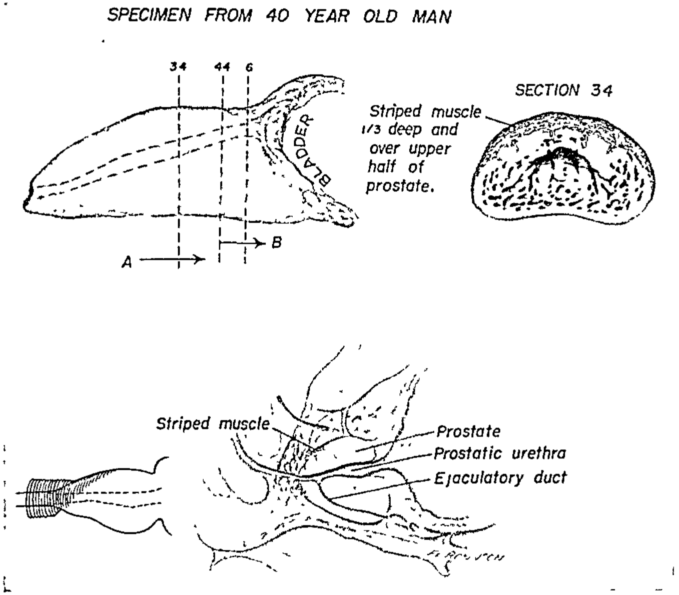
SPECIMEN FROM 40 YEAR OLD MAN
34
44
6
BLADDER
A
B
SECTION 34
Striped muscle 1/3 deep and over upper half of prostate.
Striped muscle
Prostate
Prostatic urethra
Ejaculatory duct

FIG. 7. Drawings of specimen and cross section from 40-year-old man.

men from the 7-year-old boy, this dorsal portion clearly reached the vesical outlet. It appears to us that this extension of striped muscle toward the bladder failed to reach the outlet by roughly progressively greater distances as the age of the subjects increased. This observation suggests that the normal enlarging of the prostate is the cause of the variation. Wesson considered the fibers of the external sphincter to begin on the lateral aspects of the prostate near the vesical neck, but the findings here indicate that the dorsum contains practically all of the striated muscle near the vesical outlet and little on its sides. This striped muscle is intimately associated with the prostate; indeed, it could be considered part of it. In 1904, Wallace found striated muscle in suprapubically enucleated prostatic specimens and thought this was evidence that Freyer's prostatectomy was a total one. Striped muscle in enucleated tissue has been noted many times since, and it is now well established that such prostatectomies are not anatomically complete. The striped muscle seen in the specimens obtained by prostatic enucleation are most likely bits of the capsular muscle and especially its downward rib-like, or pincer-like, extensions into the glandular substance. The function of this striated muscle is not demonstrated by such a study. Perhaps the function is concerned with ejaculation primarily; but a voluntary cut-off of the urinary stream is known to occur in the region of the prostatic apex. As long ago as 1888, Born considered the vesical outlet the most important sphincter because plaster of Paris injected down the ureters into the bladder, both *in vivo* (dogs) and post mortem (dogs and humans) did not present a downward prostatic extension. As an example of contrary evidence, Thomson-Walker found that urine did sometimes drip from a catheter whose eye was passed barely beyond the external sphincter. At least our study shows that the striped external sphincter is not the thin iris-like, camera-shutter structure commonly portrayed in standard textbooks of anatomy. Furthermore, attempts to find this iris by gross dissection were unsuccessful when we put our preconceived notions aside. The similar study of the female human by Krantz also failed to demonstrate an iris-like sphincter. The loss of control after prostatectomy is frequently incomplete, variable in degree, and fortunately often improves spontaneously. It seems certain that operative damage to this striated muscle might vary greatly, particularly because of its thickness and extent. If it were a thin, iris-like structure, damage of any significance would seem likely to be a complete division with severe disturbances and small hope of spontaneous improvement.

PART 2: RADIOGRAPHIC OBSERVATIONS OF SPHINCTERIC ACTIONS

In February 1953 we attempted to make motion pictures of the fluoroscopic image of men voiding radiopaque fluid. This was technically not successful, but in the following month we were able to obtain two exposures per second using the Fairchild magazine and a general technique employed by Draper and Siceluff. Benjamin and his associates have succeeded in making beautiful cine-x-rays which are more dramatic and facile in demonstrating the dynamics. However, the exposures made with the Fairchild apparatus do show, as far as we can determine from comparisons, the same actions.

Our first study was of a normal 52-year-old man voiding 70 per cent urokon which had been placed in the bladder through a transurethral catheter. The semilateral exposures made with the subject standing demonstrated an impressive rise of 1½ inches in the vesical base immediately preceding the voluntary stopping of the stream (fig. 8). A small projection of opaque fluid remained at the vesical outlet for a brief time while the remainder of the urethra was promptly emptied. The bladder changed shape. Similar observations were made of a

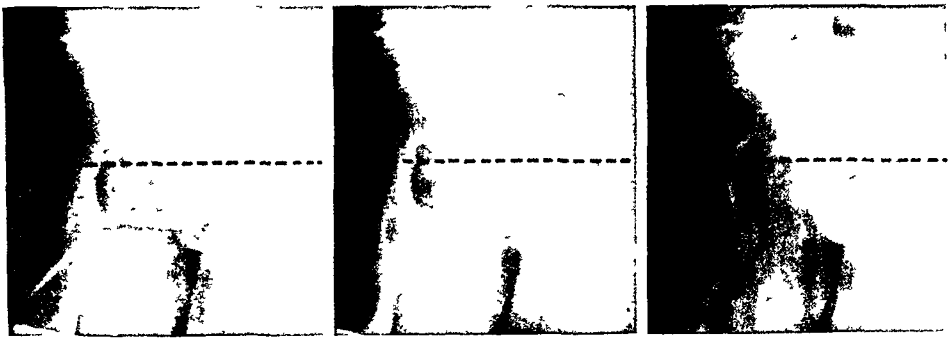

FIG. 8. Radiograph during voiding (left), voluntary interruption of urinary stream (center), and resting film (right). This 52-year-old normal man had a rise of 1½ inches by the vesical base. (N.Y.H. No. 600294.) Note common levels of base in voiding and resting films.

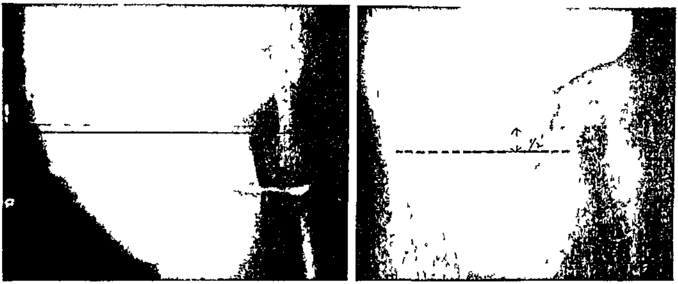

Fig. 9 One year after radical perineal prostatectomy, this patient with excellent control exhibited only a half inch rise in vesical base on voluntary interruption of stream (N.Y H. No. 601649)

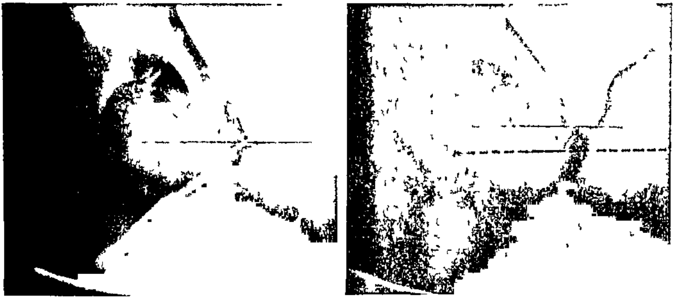

Fig. 10. After radical perineal prostatectomy, this patient exhibited a half inch rise in vesical base on interrupting stream His control was permanently quite poor but not absent (N Y H No. 620797.)

patient with excellent urinary control following a radical perineal prostatectomy by Young's technique The vesical base rose only a half inch on interrupting the stream (fig 9). Another patient after the same operation was partially and permanently incontinent (leakage on only moderate stress and necessitating protective pads during the day). In his radiographs (fig. 10) the vesical base could be seen to rise half an inch on stopping. After the transurethral removal of 70 gm. of benign hyperplasia of the prostate, a later patient was permanently partially incontinent despite exercises, dilations, instillations, and oral drugs over a period exceeding 2 years. However, this man was, and is, able to make a showing of perfect urinary control The base of his bladder rose three-fourths of an inch when the stream was voluntarily interrupted under show conditions (fig. 11) Another patient completely incontinent 3 years after a total perineal prostatectomy (for massive hypertrophy, so the seminal vesicles and bladder neck were not excised) had a vesical base which rose one-quarter inch on attempting to stop (fig. 12). Observations on still another patient with prostatic enlargement revealed no mobility of the base either before or after a perineal conserva-

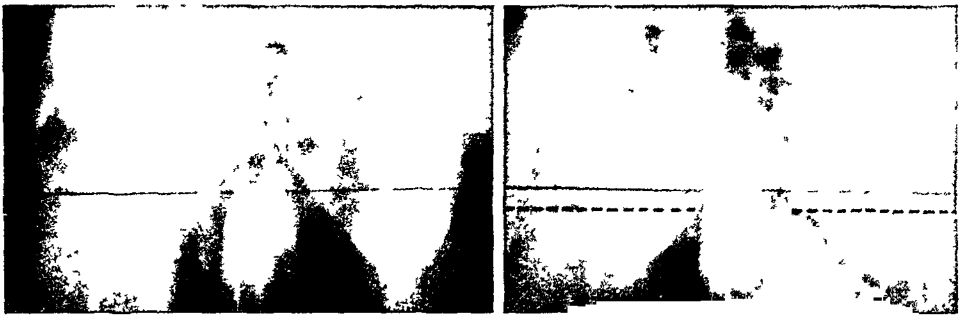

FIG. 15. Nine months later same patient (fig. 14) (N.Y.H. No. 413300) had only mild stress incontinence and exhibited 0.6 inch excursion of clips, as viewed in anteroposterior projection.

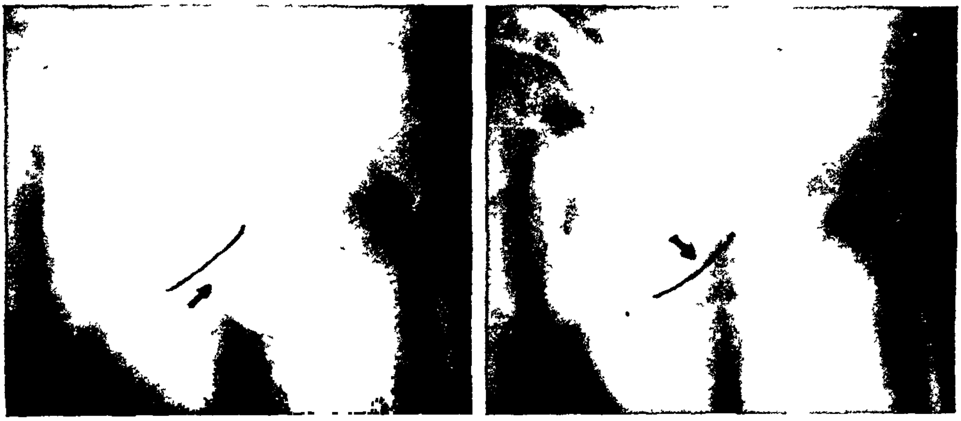

FIG. 16. Eleven days after perineal enucleation prostatectomy, opaque clip on external sphincter of this continent patient exhibited an *upward* excursion of three-fourths inch on interrupting the stream. Black line is edge of pubic ramus. (N.Y.H. No. 681049.)

second after the stop command demonstrated a complete cut-off at the vesical outlet (fig. 18). He and a second subject did have some difficulty initiating the stream, and on stopping some contrast remained in the prostatic urethra. The action of the bulbocavernosus muscles could account for the prompt emptying of the distal urethra. Lewis has told us of 3 patients with complete avulsion of the external sphincter who were treated by reapproximation of the urinary lumen across the defect, facilitated by mobilization of the bulbous urethra as necessary. He reports that none were incontinent but that once they started the urinary stream they were unable to interrupt it until the bladder was empty. Nesbit observed a man with a localized lesion of the cauda equina which, by neurological evidence, destroyed the function of one pudendal nerve. After surgical section of the other nerve his patient could void normally, whereas before this section he could void only incompletely with straining. Nesbit also mentioned the fact that Lapides had blocked both pudendal nerves of normal individuals without making them incontinent. If the external sphincter alone interrupted the stream, a thick, more or less cylindrical projection of contrast medium into the prostatic area might be expected to be noted on the films made immediately at the time of the interruption by our normal subjects. This was not present;

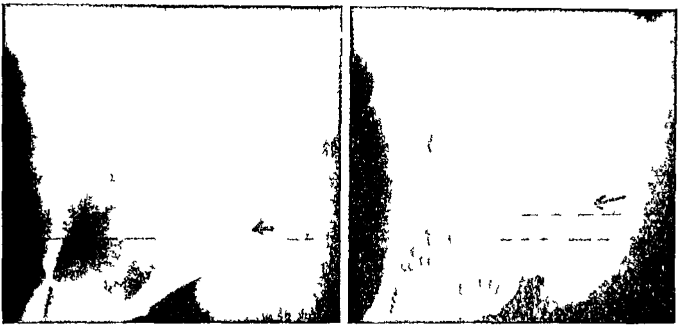

FIG 17 After open perineal biopsy of prostate clip on external sphincter of this perfectly continent patient moved *upwards* 1 inch on interrupting stream (N Y H No 681208)

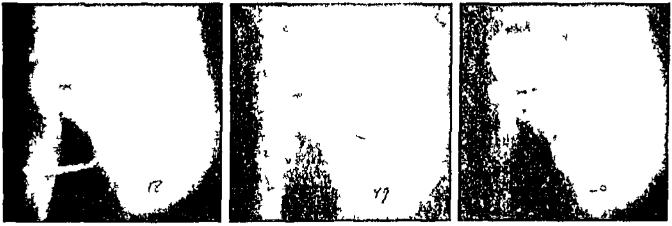

FIG 18 After transurethral infiltration of external sphincter with novocain this normal man had grossly good control, and cut off was at vesical outlet (N Y H No 603238)

but a thin, tapering projection was usually seen (fig 8) If the vesical outlet became thicker as the vesical base rose (or, more properly, as the lower limit of the contrasting accumulation in the bladder rose), then a thin, tapering projection might be expected Such reasoning suggests that the vesical outlet changes in thickness and might therefore have action similar to that of a Chinese woven finger cuff Certainly the evidence was strong that the vesical content was normally held at the vesical outlet The observations of many other investigators also indicate this Furthermore, the vesical outlet normally closes at ejaculation, since semen is not discharged into the bladder normally but often is after the vesical neck has been weakened or thinned, as after transurethral resection

SUMMARY

The external sphincter of striated muscle in four normal men consisted of a *thick ring around the membranous urethra which spread over the apex of the* prostate In fact, the muscle constituted nearly all of the prostatic capsule for at least the first seven millimeters This muscle extended toward the bladder as the dorsal part of the prostatic capsule but was interrupted in the basal region Although only four specimens were examined, it seemed that this dorsal extension more nearly reached the vesical outlet, the younger the subject. This striated muscle sent frequent extensions down into the glandular substance in a somewhat rib-like pattern. A clearly defined circumferential band of either smooth or striated muscle was not found at the vesical outlet. In short, the external striated sphincter was thick and extensive, not a thin, iris-like structure.

Radiographic studies indicated that the usual abrupt elevation of the vesical base on voluntarily interrupting the stream was not essential for perfect continence. After perineal exposure of the prostate, our few observations suggest that mobility of the levator ani muscles may be of some importance in maintaining excellent control. The external sphincter of continent men moved upwards and downwards for a surprisingly great distance (one inch, more or less) while the subject voluntarily started and stopped the stream. This new observation does not fit the popular conception of a sphincter inside a fixed triangular ligament. Inactivation of the external sphincter of continent men did not cause gross incontinence, but we suspect from our few observations that some subtle changes did result.

We hope these studies may add a little useful information toward the correction of postprostatectomy incontinence.

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The Journal of Urology
Vol 75 No 2 February 1956
Printed in U S A

TESTICULAR DYSGENESIS IN RELATION TO NEOPLASM OF THE TESTICLE

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In a previous histopathologic study of cryptorchid testes,[1, 2] evidence of testicular maldevelopment was encountered frequently enough to suggest that testicular dysgenesis is of etiologic significance in some cases of cryptorchidism It then followed that congenital imperfection of the testis may also be etiologically related to testicular neoplasm This consideration is based upon the fact that the incidence of testicular tumor is significantly greater in undescended than in scrotal testes[3-6] Moreover, there is reason to suspect that constitutional inferiority rather than abnormal location may predispose a testicle to tumor formation[1, 3]

With a view toward seeking evidence of defective gonadogenesis in testes involved by new growth, a series of tumorous testicles was studied histologically The presence of microscopic evidence of testicular dysgenesis in a significant proportion of specimens and its absence from normal scrotal testicles[9] suggest that teratological factors may be of etiologic importance in certain testicular neoplasms

MATERIAL AND METHOD

Microscopic sections, usually multiple, from 42 primary testicular tumors were examined These had been prepared from fresh surgical material which had been routinely fixed in formalin and stained with hematoxylin and eosin Of 42 neoplasms, 26 were seminomas and 16 were malignant teratomas While the patients ranged in age from 18 months to 70 years, 41 were beyond the prepuberal age No patient presented manifestations of abnormal sexual development The tumor-bearing testicle was scrotal in location in 38 instances and undescended in 4 It was right-sided in 26 and left sided in 16, the proportion of seminomas to teratomas being approximately the same in each group

Homolateral testicular tissue uninvolved by tumor was available for study in 30 cases (19 seminomas, 11 teratomas) In 3 of these the affected testis was cryptorchid The uninvolved parenchyma was systematically scrutinized for

Accepted for publication July 20, 1955

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evidence of testicular dysgenesis. As previously described,[2] this is recognized by the presence of: 1) various degrees of tubular immaturity after the prepuberal age; 2) germinal aplasia (total absence of spermatogonia not attributable to postnatal noxious influences).

OBSERVATIONS

Foci of seminiferous tubules of the prepuberal type (containing undifferentiated cells rather than mature Sertoli cells) were encountered in 6 of the 30 cases in which testicular tissue, uninvolved by tumor, was available for study. Of these, 5 were adults and one was an 18-month-old infant.

Of the 5 adult testes containing immature tubules (table 1), 3 were from a group of 19 seminomas and 2 from a series of 10 teratomas. The tumor in the infant was also teratomatous. Two of the 5 adult tumorous testicles showing immature tubules were maldescended and in each instance seminoma was present. Of considerable interest is the fact that one of these 5 neoplasms developed in a 21-year-old man whose testicle had been brought down surgically to the scrotum at the age of 11 years (case 1).

As encountered in the testes of 5 adult patients with testicular neoplasm, undeveloped seminiferous tubules presented certain constant, as well as variable, characteristics. In each instance they were found in groups rather than as single structures (figs. 1 and 2). An occasional focus of tubules was compact, circumscribed and nodular in appearance (fig. 2). The tubules were small, contained no definite lumens and were surrounded by a thin delicate basement membrane which at times showed slight thickening. The diameters of the tubules ranged between 50 and 96 microns in circular cross-sections.

The cellular content of the tubules was abundant and consisted exclusively of undifferentiated cells. Spermatogonia were absent. Individual cell borders were not distinct and the cytoplasm was eosinophilic, fibrillary and often vacuolated. The most striking and characteristic aspect of the tubules was their nuclear composition which caused them to contrast sharply with adjacent mature tubules. The nuclei were more numerous and more darkly stained than those of neighboring tubules. In some instances the tubules appeared densely packed with nuclei while in others the nuclei were peripherally distributed in one or two layers beneath the basement membrane. The nuclei were usually round or ovoid, with a sharp nuclear membrane. Occasionally they were narrow and elongated with a tendency to be arranged at right angles to the limiting membrane (fig. 2).

TABLE 1. *Neoplastic testicles showing testicular dysgenesis*

Case No.	Age	Nature of Tumor	Location
1	21	Seminoma	Scrotal*
2	25	Teratoma	Scrotal
3	31	Seminoma	Abdominal
4	37	Teratoma	Scrotal
5	39	Seminoma	Abdominal

* Orchiopexy performed at age of 11 years.

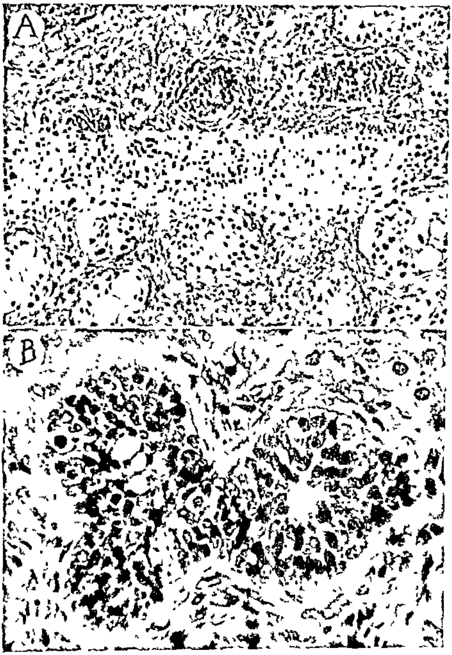

FIG. 1. Case 2. *A*, group of immature seminiferous tubules in nontumorous portion of scrotal testicle of 25-year-old man with teratoma. Tubules are smaller and contain many more nuclei than adjacent mature tubules with which they contrast sharply. *B*, high power magnification of same immature tubules. Numerous, darkly stained nuclei are typical of undifferentiated cells. Nucleoli and spermatogonia are absent. Cytoplasm is vacuolated and not distinctly outlined. A central, spheroidal, colloid-like body is present in one tubule.

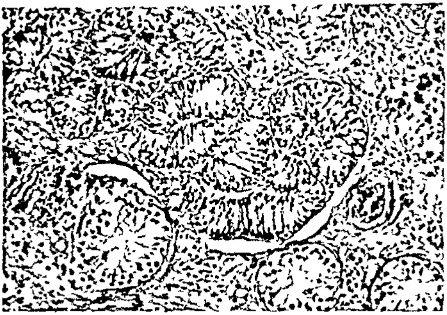

FIG. 2. Case 1. Compact, circumscribed, nodule-like group of immature tubules in uninvolved fragment of scrotal testicle of a 21-year-old man with seminoma. In comparison with adjacent mature tubules, immature tubules are smaller and contain more cells. Nuclei of latter are elongated and tend to lie at right angles to basement membrane.

Nuclear chromatin consisted of fine granular material which at times manifested a "ground glass" appearance. Distinct well-formed nucleoli were absent although small plasmosomes were occasionally identified. None of these were comparable in size or staining quality to the Sertoli cell nucleoli of neighboring mature tubules.

Colloid-like, eosinophilic, round or oval bodies resembling corpora amylacea were centrally situated in some of the immature tubules of one case (fig. 1). In another instance, similar but larger homogeneous bodies had the morphologic and staining characteristics of calcium.

The immature tubules differed in other respects from adjacent mature tubules. Evidences of degeneration, atrophy and fibrosis were absent or minimal. On the other hand, moderate atrophy of the seminal epithelium was observed in approximately one-half of the cases where nontumorous testicular tissue was available for study. Several of these also showed varying degrees of fibrosis with hyalinization. These findings were most advanced when cryptorchidism or compression by an expanding tumor had been present. Relatively normal seminiferous tubules were noted in approximately one-fourth of the specimens.

In no instance did the immature tubules appear to be connected with or to originate from adjacent mature tubules. The neoplasms and the uninvolved testicular parenchyma showed no essential differences according to whether or not immature tubules were present.

The seminiferous tubules in the testicle of the 18-month-old infant were uniformly of the prepuberal type as normally encountered during this age period. The tubules differed primarily from the immature structures of the 5 adult testes in that spermatogonia were present.

DISCUSSION

Since seminiferous tubules of the prepuberal type (containing undifferentiated rather than Sertoli cells) are not encountered in normal postpuberal scrotal testes, their presence in the testis of an adult is a manifestation of immaturity. In the absence of a recognizable constitutional, metabolic or endocrine disorder this finding is indicative of defective gonadogenesis (testicular dysgenesis).[1, 2] The absence of spermatogonia from these tubules, not attributable to local or systemic noxious influences, is further evidence of a congenital developmental defect.

Since the amount of nontumorous testicular tissue available for study was often meager, it is likely that dysgenetic lesions may have escaped detection in some instances. Under these circumstances the occurrence of histologic evidence of dysgenesis in 5 of 29 adult tumor-bearing testicles is probably an underestimate of its actual incidence. Nevertheless, the observed association between testicular maldevelopment and neoplasm is impressive enough to suggest a relationship of more than coincidental significance. While the etiology of testicular cancer is unknown, the importance of relevant or contributory factors is self-evident.

A similar association between testicular dysgenesis and cryptorchidism was established in a previous report[2] where it was suggested that congenital imperfection of the testicle may be an etiologic factor in certain cases of maldescent The combined observations bear directly on the relationship between cryptorchidism and testicular neoplasm, especially since the tell-tale immature seminiferous tubules are identical in both studies The fact that the tumor bearing testicle was maldescended in 4 of the 42 cases in this series is consistent with similar incidences reported in other studies [3, 6]

As aforementioned, there is reason to believe that an inherent defect of the testis itself, rather than its ectopic location, may predispose the undescended testicle to neoplasia The present studies suggest that tubular immaturity in an adult's testicle, regardless of its location, may represent an anatomical expression of such a defect It would thus appear that the same congenital imperfection which favors maldescent may also increase the likelihood of tumor development Moreover, similar considerations may explain the occurrence of tumors in testes years after they had been placed surgically in the scrotum This has been recorded in the literature[7] and was encountered in 2 cases of the present series, case 1 (table 1) underwent orchiopexy at the age of 11 years and seminoma developed in the same testicle 10 years later Characteristic immature tubules were found in the nontumorous portion The second case was that of a 58-year old in whom seminoma developed in the testicle which had been subjected to orchiopexy when the patient was 15 years of age In this instance uninvolved testicular tissue was not available for study

TESTICULAR DYSGENESIS AND TUBULAR ADENOMA

Certain types of immature seminiferous tubules strongly resemble, especially under low power magnification, a lesion first described by Pick[8] as tubular adenoma The resemblance applies particularly to foci of undeveloped tubules which are sharply circumscribed, compact and nodule like in appearance (fig 2) Differentiation depends primarily upon histologic criteria

As described and illustrated by Pick,[8] Lecène and Chevassu,[9] Scully and Parham[10] and Stalker and Hendry,[11] tubular adenomas in the human testicle consist of localized areas of adenomatous hyperplasia originating from the Sertoli cells of adjacent mature seminiferous tubules Their similarity to compact groupings of immature tubules is based upon the nodular appearance, the closely set clusters of small tubules containing numerous well stained nuclei and ill defined lumens, the absence of germinal cells, the occasional intratubular, spheroidal colloid-like bodies and the sparse intertubular connective tissue stroma

Points of difference include the over-all dimensions of the lesion and the nuclear

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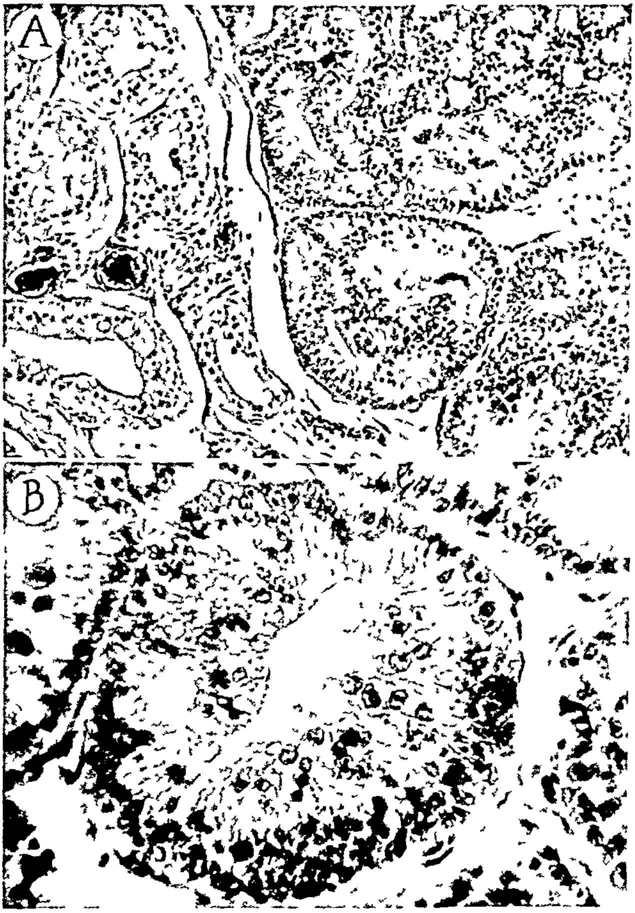

FIG. 3. *A*, small tubular adenoma in scrotal testis of 73-year-old man who was subjected to bilateral orchiectomy because of inoperable prostatic carcinoma Compact group of small adenomatous tubules (right) contrasts with larger seminiferous tubules (left). Except for moderate atrophy of seminiferous epithelium and slight tubular fibrosis, testes were otherwise normal. *B*, high power magnification of adenomatous tubules. They are lined by Sertoli-like cells with characteristic vesicular nuclei and well-formed nucleoli. Compare with undifferentiated cells of immature seminiferous tubules in figure 1.

characteristics of the tubular cells. The adenomas are usually larger, visible to the naked eye and range in size from a few millimeters to that of a bean. Their tubular epithelium is composed predominantly of Sertoli cells, each nucleus of which contains a large, distinct nucleolus (fig. 3, *B*). However, some of the nuclei are of the smaller undifferentiated type lacking nucleoli. In contrast, none of the nuclei of the immature tubules in the present or previous studies[1, 2] contained well-formed, typical nucleoli. In some cases, small plasmosomes were observed indicating a lesser degree of immaturity than that present in the totally undifferentiated cells but in no instance were the characteristic large nuclei and nucleoli of Sertoli cells found. A further distinguishing feature is said to be the presence of gradual transitions between adenomatous tubules and those of adjacent testicular tissue. These were not encountered in this study.

Because of the superficial resemblance between tubular adenomas and focal aggregations of immature seminiferous tubules, it is not unlikely that these lesions may be mistaken for one another From an analysis of published data pertaining to tubular adenomas it appears that this is probably true, since nuclear and nucleolar detail are often inadequately described

Pertinent to the principal thesis of the present investigation are the findings of Dixon and Moore [6] In a study of nearly 1000 testicular tumors, these investigators found 4 (of which 2 were cryptorchid and 2 were scrotal) to be associated with tubular adenomas The latter were regarded as incidental tumors of no clinical significance It was stated that their structure closely resembled that of the immature testis and that they probably arose from immature testicular remnants From the published illustrations, the lesions appear to be quite similar to, if not identical with, some of those encountered in this study Under these circumstances, the observations of these workers are consistent with the conclusion that testicular dysgenesis bears a relationship of undefined significance to neoplasm of the testicle

SUMMARY AND CONCLUSIONS

Circumstantial evidence suggests that an inherent imperfection of the testicle may predispose it to neoplasia Since tubular immaturity in an adult's testis may represent an anatomical expression of such a defect, 42 tumorous testicles were examined histologically for manifestations of this lesion (a form of testicular dysgenesis) The series consisted of 26 seminomas and 16 malignant teratomas

Foci of seminiferous tubules of the prepuberal type (containing undifferentiated rather than Sertoli cells) were encountered in 5 of 29 adult patients in which homolateral testicular tissue, uninvolved by tumor, was available for study. Despite the relatively small number of cases, the observed association between testicular maldevelopment and neoplasm is impressive enough to indicate a relationship of more than coincidental significance

It is suggested that the same congenital defect which contributes to the maldescent of a testicle may also render it more susceptible to tumor development This would account, in part, for the greater incidence of testicular neoplasm in undescended than in scrotal testes

The differentiation between focal aggregations of immature seminiferous tubules and tubular adenomas is discussed

I am grateful to Dr Sadao Otani who generously placed the files and microscopic sections of the Surgical Pathology Department at my disposal

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

USE OF SCROTAL SKIN TO COVER WOUND DEFECTS IN THE GROIN AND PUBIC AREA

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Under circumstances to be discussed, scrotal skin may be used as a primary "pedicle graft" to close large defects in the skin following removal of infected fungating tumors of the groin and pubic area. This paper presents observations on three such cases, two in which this principle was utilized for palliative control of recurrent carcinoma of the penis and another case in which a large inguinal defect remained following removal of a condyloma acuminatum.

Large fungating skin tumors in the area adjacent to the genitalia may present a problem in management because the area is usually infected, and a large defect in the skin may remain after removal of the tumor. While much can be done to decrease the amount of infection preoperatively by local and systemic antibiotics, it is impossible to control the infection completely. Under these circumstances a skin flap from the thigh or abdomen may be expected to meet with failure or with delayed healing. In contrast, the skin of the scrotum, because of its great mobility and vascularity, can be used to bridge the wound defect offering a simple and useful means of managing these cases. When the scrotum is used for this type of closure, infected lesions may be removed and a primary wound closure attempted thus eliminating a secondary procedure of skin grafting after the wound has filled with granulation tissue and cleared of infection.

CASE REPORT

A 53-year-old man (Harbor Hospital No. 114-665) was admitted to the hospital in April 1955 complaining of the strong odor of a large tumor located in the right groin (fig. 1, *A*). Twenty years earlier the patient had noted a small wart in the inguinal skin fold near the base of the scrotum on the right. This had gradually enlarged over the years until finally the odor of the lesion became unbearable and he sought help.

The history and physical examination were noncontributory except for the presenting complaint. His temperature was 100F and there was a 14 by 10 by 5 cm. cauliflower-like tumor in the right groin extending onto the lateral aspects of the right side of the scrotum where there were many draining sinuses with induration of the scrotal skin. Purulent material drained from the sinus tracts, and there were several enlarged inguinal lymph nodes on the right above and lateral to the lesion. Laboratory examinations were normal. A specimen obtained from the periphery of the tumor showed condyloma acuminatum.

When it was determined that the lesion was benign, it was decided to treat it by wide local excision and closure of the wound defect with the scrotum. Previous observation of the other two cases to be mentioned later led to acceptance of this procedure as a logical one.

Accepted for publication September 21, 1955.

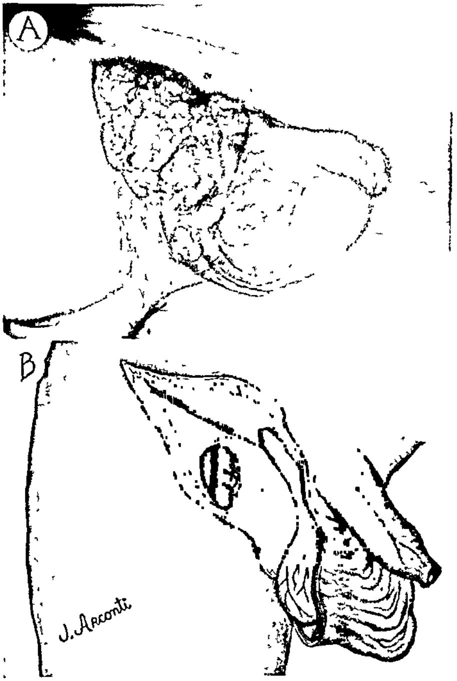

Fig. 1. Case 1 (H. H. No. 114-665). *A*, gross appearance of large condyloma acuminatum *B*, drawing of surgical defect which was closed by scrotal skin.

The patient was given sitz baths before surgery, but no antibiotics were used until the day of surgery. At the time of operation there was induration around the margin of the lesion, and the purulent drainage from the base of it had decreased since the time of admission. The tumor was removed by a wide incision which extended through relatively normal skin and subcutaneous tissue around its periphery. The inguinal and subinguinal nodes were removed *en bloc* with the tumor down to the fascia lata and the external oblique aponeurosis (fig. 1, *B*). A frozen section of the enlarged inguinal nodes removed with the specimen was negative for tumor.

The large defect in the inguinal region, which remained after removal of the tumor, was easily covered by a scrotal flap which was mobilized laterally to include the skin and dartos layers. The wound was drained through the suture line in the perineum. Postoperatively the patient received penicillin and streptomycin twice daily for 8 days. The silk skin sutures were removed on the ninth postoperative day when the patient resumed sitz baths twice a day. By the fourteenth postoperative day the wound was well healed, and most of the in-

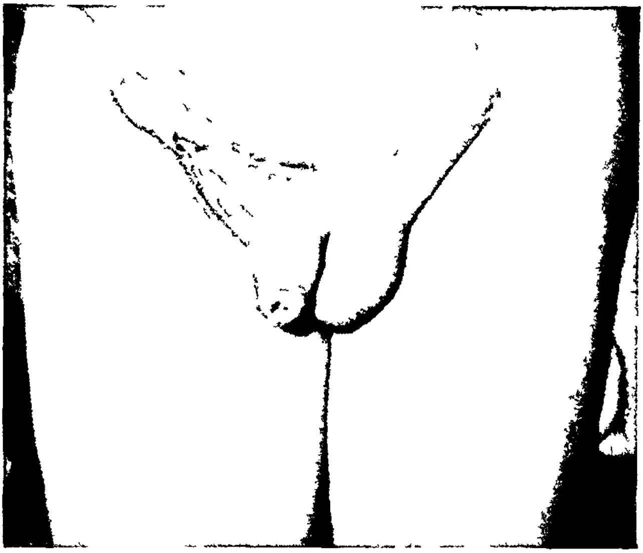

FIG. 2 Case 1 Appearance fourteenth postoperative day

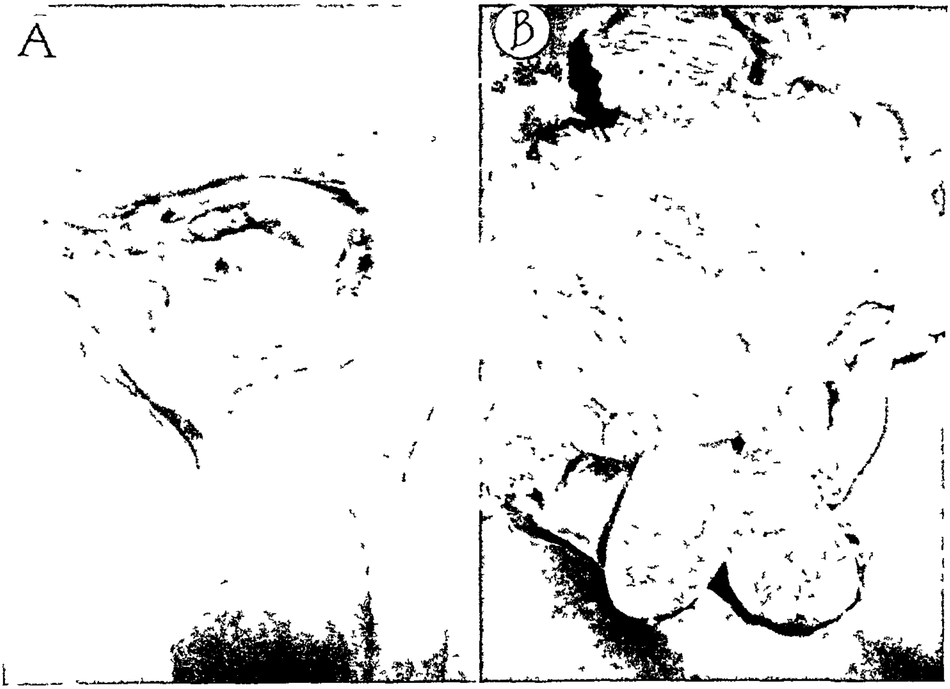

FIG. 3 Hodges' case (H C , Brady Urological Institute) A, recurrent carcinoma of penis after simple amputation B, gross specimen.

duration had subsided (fig 2) Permanent microscopic sections of the tumor and lymph nodes confirmed the original biopsy report.

The principle of using scrotal skin for this purpose was first suggested to one of us in 1948 by C. V. Hodges who used it to cover a large abdominal defect following palliative excision of a huge recurrent carcinoma of the penis in the lower

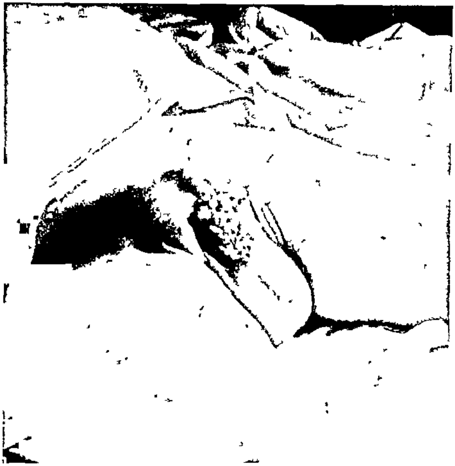

FIG. 4. Gorfain's case (C. A. W , St. John's Hospital). Recurrent carcinoma of penis after simple amputation.

abdomen. Hodges' case* came to the hospital for palliation only. Examination revealed a tremendous fungating neoplasm occupying the suprapubic area (fig. 3, *A*). Biopsy demonstrated that it was recurrent carcinoma of the penis for which the patient had had partial amputation some years previously. This was treated by a radical local excision including the skin and the anterior abdominal structures down to and including the rectus fascia. The whole lesion and a segment of the presymphysial skin and both testes made up the specimen (fig. 3, *B*). Hodges then mobilized the scrotal skin and pulled it upward to cover the defect leaving the patient with a permanent perineal urethrostomy. The result was dramatically successful as the wound healed without much difficulty. There was some ischemia and necrosis of a portion of the scrotal skin edge, but the large defect was closed. The presence of infection did not seem to be a barrier to the successful result of this operation.

A second case was under the care of A. D. Gorfain with the same problem of recurrent penile carcinoma limited to the pubic area. One of us saw the patient with him in March 1953 and recalling Hodges' success, suggested that the same principle be applied in this second patient. Gorfain's case† was a 91-year-old man who many years earlier had had a simple amputation for carcinoma of the penis. He came for palliative treatment because of a local recurrence. He had stenosis of the urethra, and a foul fungating pubic mass (fig. 4). This was successfully treated by perineal urethrostomy, local excision of the mass, and primary closure of the defect with the scrotum. There was "complete healing and no further trouble with the genitourinary tract."

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* This case is included through the courtesy of Dr. Clarence V. Hodges, University of Oregon Medical School, Portland, Oregon

† This case is included through the courtesy of Dr. A. D. Gorfain, West Los Angeles, Calif.

It was knowledge of the successful results of these first 2 cases that led to boldness in handling the present case reported in detail.

SUMMARY AND CONCLUSION

Extensive wound defects in the lower abdomen and inguinal regions may be closed primarily with "pedicle grafts" of scrotal skin which can be mobilized relatively great distances with good wound healing in the presence of infection. The method employed is not intended to be desirable where good cosmetic effects are sought but should be restricted to cases similar to those presented offering such patients a relatively short period of hospitalization. The same principle could be employed in rare cases where radical local excision of the penis *is necessary in conjunction with extensive inguinal node dissection for carcinoma* of the penis. When perineal urethrostomy is employed in these patients, the scrotal skin could be mobilized in part to aid in closure of the wound defect.

Three patients treated in this manner are presented. Two of them had recurrent pubic skin lesions from carcinoma of the penis and one had a large fungating condyloma acuminatum in the right inguinal region.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

INTRASCROTAL ADENOMATOID TUMOR: CASE REPORT

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Adenomatoid tumors are a group of uncommon, benign neoplasms found within the extratesticular tissues of the male or, rarely, on the serous surfaces of the uterus, tubes and ovaries. They are of importance chiefly because they frequently present as scrotal tumors in young men, a circumstance which tends to produce an erroneous impression of testicular malignancy. The following case illustrates the major features of these tumors.

CASE REPORT

A 34 year-old married white man first noticed a swelling of the left testicle 2 weeks prior to his examination. He gave no history of previous surgery or injuries. The remainder of his medical history was not relevant. Physical examination was negative except for the presence of a firm, smooth, round nodule, 2 cm. in diameter, just posterior to the lower pole of the left testicle. The nodule was nontender, separate from the testis, and apparently attached to the globus minor of the epididymis.

The patient was admitted to the hospital where re-examination, chest x-ray, urinalysis and blood counts failed to disclose any further abnormalities. At surgery the nodule was found to be attached to the globus minor; it was dissected from the testis proper with comparative ease. A frozen section of the nodule was interpreted as showing possible malignancy. Orchiectomy was therefore performed. The patient made an uneventful recovery.

The specimen consisted of a small, spherical mass of firm tissue, 1.5 cm. in greatest diameter. The external surface was almost completely covered by a focally roughened gray membrane. Cut sections revealed firm, grayish-white whorled surfaces.

The testis and epididymis were both grossly and microscopically normal.

Histologic sections of the tumor showed a rather dense fibromuscular stroma, through which were dispersed numerous small angular spaces with rather irregularly disposed cell linings. These structures resembled vascular sinusoids more than glands; their lumens however were quite clear. The cells varied in shape from low columnar to flattened or spindle forms. Their cytoplasm was acidophilic and frequently vacuolated. The nuclei were medium sized, ovoid, with finely granular chromatin and distinct basophilic nucleoli. The "solid cord" pattern of epithelial like cells was present in foci near the center of the tumor; only rarely were there configurations suggestive of mesothelial proliferation. A layer of compressed fibrous tissue outlined most of the periphery of the nodule. The diagnosis of adenomatoid tumor was made on the permanent sections.

Accepted for publication June 14, 1955.

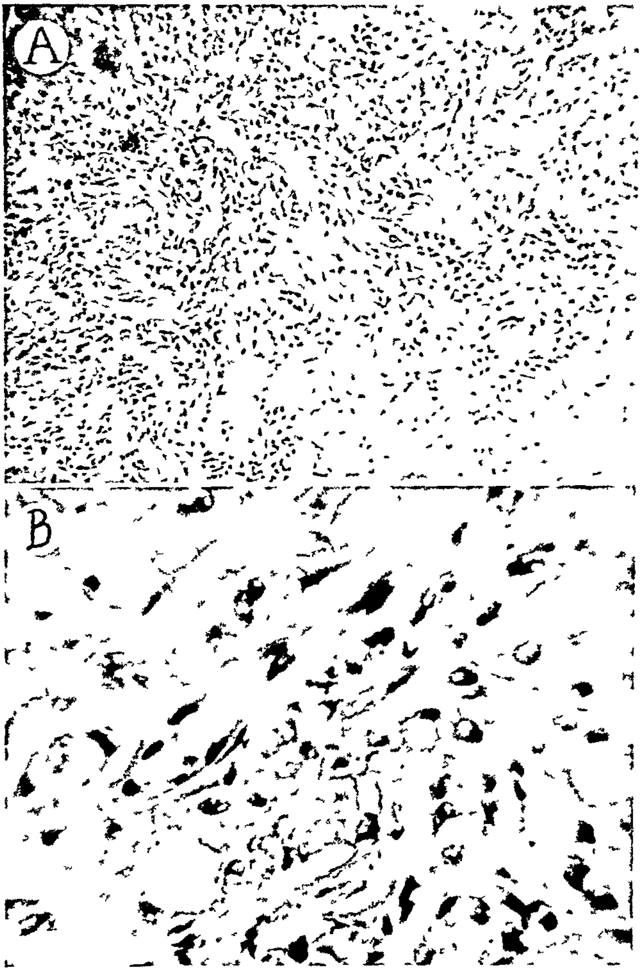

Fig. 1. Photomicrographs. *A*, typical field, low power. Angiomatoid pattern predominates *B*, area where progressive vacuolation of cells is evident, high power.

COMMENT

The adenomatoid tumor is most commonly encountered as a small, firm, nodular mass attached near the lower pole of the epididymis. Often there is a history of its presence for several years without any change in size or other symptoms.

Histologically it may have a cellular, bizarre pattern suggesting invasive adenocarcinoma. Further study generally reveals the presence of a variable mixture of epithelial-like or adenomatoid configurations: solid cords of cells, gland-like structures and irregular slits or angular spaces. Dixon and Moore have traced the development of these latter forms by progressive vacuolization of the solid cords of cells. Usually at least traces of each of these can be found distributed through a fibrous stroma which may contain muscle and lymphocytic aggregates.

The origin of the adenomatoid tumor is in dispute. Although derivation from mesonephric remnants, from lymphangioid elements and from epithelium have each been favored by different investigators, the current trend is toward acceptance of a mesothelial origin. Ambrose recently reviewed the evidence supporting the various points of view.

One point worth emphasizing is the benign behavior of these tumors; no case has ever been reported in which the neoplasm developed any malignant characteristics.

SUMMARY

An additional case of adenomatoid tumor is presented. The clinical and pathologic features of these tumors are briefly reviewed.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

ANASTOMOSIS OF THE VAS DEFERENS: AN EXPERIMENTAL STUDY. I

STANWOOD S. SCHMIDT

The classical paper by O'Conor in 1948[1] on anastomosis of the vas deferens was the first to publicize extensively the fact that this could be a relatively successful operation. Since then many surgeons have attempted the operation and reports of successes are common.[2-7]

The technique of the operation varies somewhat with different authors. An analysis of these reports and a familiarity with the operation reveal certain principles which favor success. Previous section of the vas at a location high in the scrotum permits an easy anastomosis compared with the difficulty encountered in attempting an anastomosis of the convoluted portion of the vas. The anastomosis should be made without tension. This is difficult where a long segment of vas has been excised previously. End-to-end anastomosis is more successful than lateral anastomosis. Use of a removable splint of a nonabsorbable material seems to give greater success.[1, 3, 6, 7, 8] Gentle handling of tissue is particularly important when dealing with a structure as small as the vas. The blood supply to the vas must be left intact. This is done by resecting as little tissue as possible from the tied ends.[3] The prophylactic use of antibiotics is justified. Careful attention must be given to asepsis.

The principles behind the use of a splint deserve mention. The purposes of this are first to align the lumen of the vas and to supply a guide for the epithelialization of the point of anastomosis, and secondly to splint the vas in such a manner as to prevent kinking at the point of anastomosis and subsequent partial separation. Although wire has been used extensively as a splint, it seems to me that its rigidity and lack of elasticity are disadvantages when compared with a pliable, nonmetallic material such as dermal, silkworm gut or nylon. Nonremovable splints such as catgut or various tubes present the chemical and mechanical disadvantages of a more permanent foreign body.

A moderate variation of opinion exists as to the proper length of time that a splint should be left in. This must be of sufficient duration that complete epithelialization and at least partial muscular regeneration across the point of anasto-

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Accepted for publication July 29, 1955.

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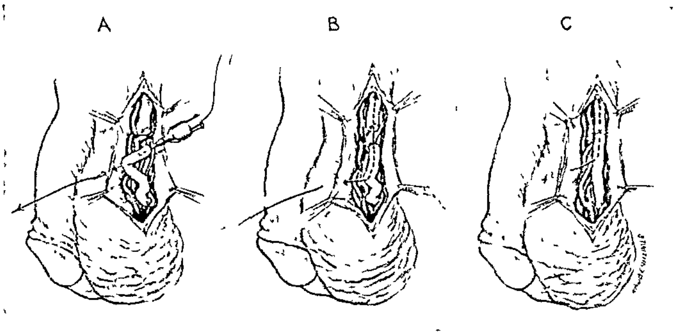

FIG. 1

mosis shall occur. Premature removal would leave a weak, poorly supported anastomosis and could contribute to failure of the operation.

I have performed successful anastomoses of the vas deferens as determined by the presence of sperm in the ejaculate upon five consecutive azoospermic cases. All of these men had fathered children prior to vasectomy. A nylon splint was used in these cases. On an empirical basis the splint was left in place for a period of 5 days in four of these cases. Through a misunderstanding the splint was left in for 10 days in the remaining case. Pregnancies have occurred in the wives of three of these five men. One of the five men has left the area and no further information is to be had. The fifth patient has been unable to get his wife pregnant. Although sperm are present in his ejaculate, a count of only fifteen to twenty million is found, the sperm having poor motility and showing a considerable number of abnormal forms. Testicular biopsy is now planned in this man.

In humans the size of the splint is determined by using the largest caliber of nylon that can be passed through the lumen of a No. 19 (No. 3 nylon) or a No. 20 (No. 2 nylon) hypodermic needle. In placing the splint, such a needle is passed down the lumen of the proximal vas for a distance of several centimeters, where possible. This can be done even in the convoluted portion of the vas, although for a short distance only. The needle is then passed through the wall of the vas and out through the skin of the scrotum (fig. 1, *A*). The nylon splint is threaded through this needle and fixed to the skin after the needle is withdrawn. The other end of the splint is then passed into the end of the distal vas for a distance of several centimeters (fig. 1, *B*). The ends of the vas are then approximated with interrupted sutures (fig. 1, *C*). The dilation of the proximal end of the vas, described by some authors,[9] was not noted in any of the author's cases. Local anesthesia is adequate for these cases and a hospital stay of only a few hours is necessary. Suspensories are used postoperatively in all cases.

Since success was met with by leaving a splint in for lengths of time varying from five to ten days, it seemed of interest to determine the rate of healing of the anastomosed vas. Previous experimental work was lacking; therefore, the following study was carried out.

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MATERIALS AND METHODS

Ten young male dogs were used. Bilateral anastomosis was done in each case, making a total of twenty anastomoses performed and studied. The vas was exposed through a high scrotal incision. A section 1 cm. long was removed as in a standard vasectomy and an end-to-end anastomosis was performed over a nylon splint (No. 000 dermalon). The walls of the vas were approximated with three interrupted sutures of 4-0 chromic catgut, these being placed to avoid the lumen of the vas. No attempt was made to make the splint removable nor was any attempt made to study other splinting materials. At the end of specified periods of time the section of vas containing the anastomosis was removed and serial sections were made of this.

EXPERIMENTAL OBSERVATIONS

The anastomoses were removed and examined after periods of 3, 5, 7, 9 and 16 days. At 3 days granulation tissue was present, but there was no evidence of epithelial or muscular regeneration. After 5 days, epithelial regeneration was seen to be present but did not join the two ends. No muscle fibers were seen to be bridging the site of anastomosis. After 7 days, however, the epithelium was seen to cross the point of anastomosis in all cases. Early muscle regeneration was seen. In one instance, epithelium was seen to be growing down into the suture line at right angles to the direction of the vas. In this case there was slight separation of the one side of the anastomosis. After 9 days the epithelium was again seen to be intact. Muscle regeneration was active and was pronounced in the longitudinal muscle layer. After 16 days muscle regeneration was almost complete. The inflammatory reaction which was present to varying degrees in the earlier specimens had subsided except around the sutures.

A number of interesting observations were made from the entire series. In no case was any reaction to the splint seen. In several cases approximation was shown to be imperfect in spite of every attempt being made to secure close approximation. Inflammatory cells mixed with spermatozoa were present in the resulting gaps. It was impossible to tell to what degree, if any, the spermatozoa added to the inflammation. No sperm were present in the suture line of the specimens examined at the end of 16 days, where healing was almost complete. Reaction to the catgut was marked in all instances.

DISCUSSION

A survey of the reports of successful anastomosis of the vas reveals that different authors empirically favor leaving the splint in for a period of six to ten days. The experimental work which I have presented would indicate that epithelial regeneration will be found by the seventh postoperative day but that regeneration of the muscle takes twice as long. The anastomosis should be completely epithelialized and reasonably strong by the tenth day The absence of tissue reaction to a splint such as nylon would permit its being safely left in for that length of time

The presence of sperm in the suture line in several specimens shows the importance of securing a close approximation of the ends of the vas Friedman and Garske[10] have shown that sperm can cause a granulomatous reaction in the tissues and thus any such extravasation is to be avoided The human vas, being approximately twice the size of that of the dog, is easier to suture and should be more easily approximated

Although fine chromic catgut sutures were used in the experiment, they are not the best for this purpose A fine, nonabsorbable suture swedged on a needle would seem more desirable and may result in a greater percentage of success Silk eye suture material (6-0) seems well suited to this purpose

The finding of a large number of nonmotile and abnormal sperm in the ejaculate after anastomosis of one patient who has children by a previous marriage points out the desirability of taking a testicular biopsy at the time the anastomosis is done

SUMMARY AND CONCLUSIONS

Anastomosis of the vas deferens is an operation which can be performed successfully in the vast majority of cases in which a previous elective vasectomy has been done

Division of the vas high in the scrotum with excision of only a small segment of vas at the time of sterilization favors success in a subsequent anastomosis

Not infrequently elective vasectomy is a symptom of a failing marriage and is done in hopes of saving it Should divorce and remarriage ensue, many of these men will seek surgical restoration of their fertility.

Experimental work is reported which demonstrates the time required in the dog to effect healing of the point of anastomosis Epithelial regeneration is complete after 7 days Muscle regeneration is active after 9 days and is complete after a period of 16 days On this basis, and since the time for healing in the dog and in the human is closely comparable, the author recommends leaving the splint in for a period of 10 days, although successes are reported when the splint was left in only 5 days

Nylon is an excellent splinting material, because of its pliability and elasticity and because of the absence of tissue reaction to it

An atraumatic method of placing the splint in the vas utilizing a hypodermic needle and a nylon splint is described

The author wishes to acknowledge the assistance of Dr Robert Morris, who prepared and reviewed the slides, and the indispensable assistance of several other friends who secured the animals and cared for them

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

THE PROPHYLACTIC USE OF CHLORAMPHENICOL IN TRANSURETHRAL RESECTIONS OF THE PROSTATE GLAND

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The use of antimicrobial drugs for prophylaxis may be a factor in the increase of strains of bacteria that are resistant to these drugs.[1-3] In addition, many serious toxic reactions have resulted from the use of antimicrobial agents.[4] Therefore, before the use of antibiotics for prophylaxis is justifiable, a beneficial result of such usage that is of sufficient magnitude to compensate for these theoretical disadvantages must be demonstrated. This has been done with the use of penicillin therapy to prevent recurrences of rheumatic fever and with the use of sulfadiazine to prevent epidemics of plague.[5, 6] On the other hand Lepper, Jackson and Dowling[7] have shown that prophylactic antimicrobial therapy in patients with tracheotomies has a net effect that may be detrimental to the patient.

Creevy and Feeney have reported excellent results with the routine use of chlortetracycline, with the combination of chloramphenicol and gantrisin; and with oxytetracycline before transurethral resection of the prostate gland.[8] They feel that this prophylactic antimicrobial therapy has reduced their operative mortality and morbidity, decreased postoperative febrile reactions, and decreased the number of positive postoperative blood cultures.[8] These conclusions are open to some question because "a regimen was abandoned either when sufficient data concerning a drug had accumulated, when it became evident that it did not influence the incidence of bacteremia, or when it caused too many reactions." Therefore, the "controls" were operated upon in some cases many months before the patients who were given antibiotics. During these months it is not unreasonable to assume that improvements in operative technique, postoperative care, and particularly in the use of different solutions for irrigation, may

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Accepted for publication September 21, 1955.

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have accounted for some of the differences between the two groups of patients.[9] The report of Strom and Thompson[10] regarding the routine use of sulfathiazole before transurethral resections also used, as a control group, patients who had been operated on the year before the study was done. Although the 100 patients to whom sulfathiazole had been given did appear to have a slightly lower incidence of high fever, the differences between the two groups was not striking and no deaths resulted in either the treated or the untreated patients. Furthermore, the studies of Gaudin, Zide and Thompson[11] and of Bulkley, O'Conor and Sokol[12] did not result in their making a recommendation for the routine use of antimicrobial drugs in transurethral resections of the prostate gland.

The purpose of the study to be reported was to determine if a statistically proven advantage could be demonstrated with the prophylactic use of a wide spectrum antibiotic before and after transurethral resection. In order to do this, strict alternation between the control and treated groups was observed in 100 cases of transurethral resection.

MATERIAL AND METHODS

One hundred consecutive cases of transurethral resections performed at the Milwaukee County General Hospital were studied. Strict alternation of cases was followed and 50 cases were given chloramphenicol in the preoperative and postoperative periods while 50 alternate cases were given no specific antimicrobial therapy.

Since strict alternation was used, the 100 operations were performed on 69 patients, 24 of whom had multiple resections. Patients with vesical neoplasms were not included in this series. In the treated patients, chloramphenicol was given in a dosage of 250 mg. 4 times a day for a preoperative period ranging from 1½ to 3 days. Therapy was continued during the immediate postoperative period and in some instances for as long as 3 weeks.

Chloramphenicol was chosen as the wide spectrum antibiotic for the following reasons: 1) Its activity against Proteus and Micrococcus pyogenes gives it a wider spectrum than that of the tetracyclines.[13, 14] 2) In our experience it is the best tolerated of the wide spectrum antibiotics. 3) In our experience and in our hospital it has been the safest of the wide spectrum antibiotics because it is the only one of this group in which we have not observed severe diarrhea due to M. pyogenes subsequent to its administration.[15] 4) These above reasons, in our

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TABLE 1. *Age and racial distribution of patients*

Age	Control Group		Treated Group	
	Race		Race	
	Negro	White	Negro	White
50–60		1		
60–70		11		8
70–80	1	29	1	32
80–90		8		9
Total .	1	49	1	49

TABLE 2. *Signs and symptoms of prostatism found in the treated group and the control group of patients*

Sign or Symptom	Number of Patients with Symptoms or Signs	
	Control	Treated
Nocturia	34	33
Retention	34	32
Diuria .	26	21
Dysuria .	14	25
Diminution in size and force of stream	16	17
Hesitancy	17	10
Pyuria .	12	14
Urgency	9	9
Stammering	10	6
Chills and fever.	2	4

opinion, overweighed the slight statistical change of blood dyscrasia that is present when chloramphenicol is administered.[16] All patients were given a complete examination on admission. Ages ranged from 57 to 89 years and the majority of patients were in the seventh decade (table 1). There was one Negro in each group. The symptoms and signs of prostatism of the entire group were found in the following order of frequency: nocturia, retention, diuria, dysuria, diminution in size and force of urinary stream, hesitancy, pyuria, stammering, urgency and fever. These symptoms and signs were exhibited equally in the control and treated groups (table 2). The average duration of symptoms was 25 months in the control group and 30.8 months in the treated group. The average number of preoperative instrumentations was three in both groups.

Associated diseases were present in almost all of the patients in both the control and treated groups. Cardiovascular and respiratory diseases were most common (table 3). Other associated diseases included diabetes mellitus, cirrhosis, diverticulitis of the sigmoid colon, malignancy other than in the urinary tract, bacteremia, epilepsy, epididymitis, pyelonephritis, bilateral hydronephrosis, urethral and rectal perforations, vesical diverticula and central nervous system syphilis. These associated diseases were equally present in the control

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[16] Lewis, C. N., Putnam, L. E., Hendricks, F. D., Kerland, I. and Welch, H.: Chloramphenicol (chloromycetin) in relation to blood dyscrasias with observations on other drugs. Antibiotic & Chemoth., 2: 601–608, 1952.

TABLE 3. *Preoperative complications*

Preoperative Complications	Control	Treated
Arteriosclerotic heart disease	27	29
Essential hypertension	7	5
Cerebral vascular accident	4	5
Senile psychosis	5	3
Diabetes mellitus	2	6
Arterial sclerotic heart disease	8	3
Pulmonary emphysema	2	5
Myocardial infarction	1	4
Acute epididymitis, unilateral	1	2
Central nervous system syphilis	1	2
Bilateral hydronephrosis	0	0
Proteus septicemia	0	2
Vesical calculi	0	2
Bronchial pneumonia	2	0
Cirrhosis of the liver	1	0
Diverticulitis of the sigmoid colon	1	0
Malignancy other than genitourinary tract	0	1
Atelectasis	0	1
Bronchial asthma	1	0
Idiopathic epilepsy	1	0
Escherichia coli septicemia	1	0
Rents in urethra and rectum	0	1
Pyelonephritis, acute	0	1
Vesical diverticula	1	0
Total	66	72

TABLE 4 *Preoperative drainage*

	Control Group		Treated Group	
	No of Patients	*Average* Drainage (days)	*No of* Patients	*Average* Drainage (days)
Preoperative catheter drainage	36	11.5	40	14.5
No preoperative catheter drainage	13		9	
Previous suprapubic drainage	1	365	1	365
Total	50		50	

and treated patients (table 3). Thirty-six patients in the control group and 40 patients in the treated group required an average of 11.5 days and 14.5 days of preoperative catheter drainage respectively (table 4). The amount of residual urine as determined preoperatively was similar in both groups of patients (table 5). The patients in whom multiple resections were necessary were divided by chance in the control and treated groups as shown on table 6. Three patients in the control group and 5 patients in the treated group were given other antimicrobial agents at intervals before their surgery. However, in each instance at least 5 days had elapsed before they were operated on or given chloramphenicol. The similarity between the urinalysis done on the patients

TABLE 5 *Preoperative residual urine*

Residual Urine	Control Group	Treated Group	Total
<100 cc	11	7	18
100–300	11	11	22
300–500	11	6	17
500	18	25	43
Total			100

TABLE 6 *Data on 24 patients who had more than one resection*

	Number of Patients	All Resections in Control Group	All Resections in Treated Group	First in Treated Then in Control Group	First in Control, Then in Treated Group
2 Resections	16	3	6	5	2
3 Resections	7	3	2	2	0
4 Resections	1				1
Total	24	6	8	7	3

TABLE 7. *Preoperative urinalysis*

Urinalysis	Control	Treated
Acid	33	35
Basic	17	15
Albuminuria	18	19
Sugar	2	0
Pyuria	27	27
Hematuria	18	24

in the control and treated groups can be seen on table 7. Preoperative urine cultures were taken from both groups of patients and the results are in table 8. Admission and preoperative cultures showed almost an identical bacteria flora among the two groups of patients. After the transurethral resection, the patients in each group were studied in order to determine whether the prophylactic therapy had any effect on the following: immediate postoperative complications, postoperative bacteremia, postoperative drainage period, postoperative pyrexia, postoperative hospital stay and mortality. In addition, evidences of toxicity due to chloramphenicol were sought.

RESULTS

1) Immediate postoperative complications. There were 17 immediate postoperative complications in the untreated group and 21 among the patients given chloramphenicol (table 9). The complications such as dysuria, chills, epididymitis, a perineal abscess and pyelonephritis, that might have been expected to be reduced by the administration of chloramphenicol, occurred more frequently among the treated than among the untreated patients (table 9). On the other hand, the higher incidence of complications in the treated group could

TABLE 8 *Results of urine cultures taken before operation*

Organism Cultured	Control		Treated	
	Admission urine	Preoperative urine	Admission urine	Preoperative urine
Staphylococcus albus	34	30	31	24
Micrococcus pyogenes	3	10	7	6
Hemolytic streptococcus	4	7	4	2
Nonhemolytic streptococcus	19	28	15	19
Pseudomonas aeruginosa	11	24	12	21
Escherichia coli	16	19	19	22
Proteus	6	13	5	5
Bacillus subtilis	3	1	3	3
Pseudomonas species	2	3	0	3
Streptococcus viridans	1	1	3	2
Paracolobactrum				3
Alcaligenes faecalis	2	1	1	
Diphtheroids				1
Cultures not obtained	3	1	2	
Negative cultures	2		8	3

TABLE 9 *Immediate postoperative complications*

Immediate Postoperative Complications	Control Group	Treated Group
Severe dysuria	4	6
Mild toxic reaction (urethral shaking chill)	6	6
Epididymitis unilateral	2	1
Pyelonephritis (clinical)	1	2
Hemorrhage requiring fulguration		2
Urinary extravasation	2	
Cerebral vascular accident		1
Severe toxic reaction	1	1
Perineal abscess secondary to perineal urethrostomy		1
Acute myocardial infarction	1	
Acute left ventricular failure		1
Total	17	21
No complications	33	29

not be attributed to the chloramphenicol (table 9) Four patients in the control group were given antimicrobial therapy postoperatively because of their complications (table 10) Three patients in the treated group needed additional antimicrobial therapy and it is worthy of note that the more serious infections appeared to have occurred in this group (table 10) Of particular interest was the case of acute bacterial endocarditis due to M pyogenes that developed in spite of prophylactic chemotherapy and ended fatally in spite of vigorous treatment (table 10)

2) Postoperative bacteremia Blood cultures were drawn from 25 patients during the immediate postoperative period In each instance, the culture was drawn

TABLE 10. *Postoperative antimicrobial therapy excluding "routine" chloramphenicol*

Group	No. Patients	Drug(s)	Indication(s)	Duration of Therapy
Control	1	Penicillin	Urinary extravasation	11
		Chloramphenicol	Bronchopneumonia	
		Chlortetracycline		3
		Erythromycin		11
	1	Penicillin	Urinary extravasation	5
		Chloramphenicol		
	1	Chlortetracycline	Severe toxic reaction	4
	1	Penicillin	Escherichia coli septicemia	7
		Chloramphenicol		
Total	4			
Treated	1	Penicillin	Right pyelonephritis	5
		Chloramphenicol		
	1	Chlortetracycline	Perineal abscess	5
		Penicillin	Acute endocarditis	7
		Chloramphenicol	Cerebral septic	
		Chlortetracycline	Emboli-organism	
	1	Oxytetracycline	Coagulase positive	5
		Polymyxin B	Staphylococcus aureus	
		Mandelamine		
		Neomycin		6
		Nitrofurantoin		2
Total	3			

TABLE 11. *Results of postoperative blood cultures on twenty-five patients*

Organism	Number of Patients	
	Control	Treated
Staphylococcus albus (coag. −)	2	
Escherichia coli	2	
Pseudomonas aeruginosa		1
Micrococcus pyogenes (coag. +)		1
Negative	9	10
Total	13	12

because the clinical condition of the patient suggested the possibility of a bacteremia. Four of thirteen cultures drawn in the control group were positive and two of twelve cultures drawn from the treated group yielded growth (table 11). Pathogenic organisms in the control group were E. coli whereas in the treated patients Pseudomonas aeruginosa and coagulase positive M. pyogenes were isolated.

3) Postoperative urine cultures. The postoperative urine cultures taken from the control and treated groups of patients were almost identical. In not a single instance in either group was a completely sterile specimen obtained. Almost identical numbers of patients in each group had M. pyogenes, E. coli, Proteus

TABLE 12. *Results of urine cultures taken after operation*

Organism Cultured	Control		Treated	
	Admission urine	Postoperative urine	Admission urine	Postoperative urine
Staphylococcus albus	34	27	31	24
Micrococcus pyogenes	3	8	7	7
Hemolytic streptococcus	4	5	4	3
Nonhemolytic streptococcus	19	19	15	18
Pseudomonas aeruginosa	11	27	12	22
Escherichia coli	16	18	19	21
Proteus	6	12	5	11
Bacillus subtilis	3	2	3	1
Pseudomonas species	2	2	0	3
Streptococcus viridans	1	0	3	1
Paracolobactrum				
Alcaligenes fecalis	2		1	
Diphtheroids				
Cultures not obtained	3		2	
Negative cultures	2		8	

TABLE 13. *Postoperative drainage*

Postoperative Drainage	Number of Cases		Average No Days of Postoperative Drainage	
	Control	Treated	Control	Treated
Uncomplicated urethral catheter drainage	45	47	3.9	3.9
Catheter drainage prolonged due to perineal urethrostomy	1	2	13	15
Catheter drainage prolonged due to acute myocardial infarction	1		35	
Catheter drainage prolonged due to cystostomy	1	1	27	10
Catheter drainage prolonged due to urinary extravasation	2		21	
Total	50	50		

and Pseudomonas aeruginosa which were the most important pathogens isolated (table 12). Thus, no effect of the preoperative medication on the postoperative bacterial flora of the urine was demonstrated.

4) Postoperative drainage period. The postoperative drainage period averaged 3.9 days in 45 patients of the control group. In the five other instances catheter drainage was necessary for many days due to urinary extravasation in 2 cases, perineal urethrostomy in another case, previous cystostomy in another and myocardial infarction in the other patient (table 13). The postoperative drainage period also averaged 3.9 days in 47 patients of the group who had received chloramphenicol. Prolonged drainage was necessary in 3 patients in this group. Two of these had perineal urethrostomy and the other had a cystostomy drainage.

5) Postoperative pyrexia. Table 14 shows the extent of postoperative fever

TABLE 14. *Postoperative temperatures*

Postoperative Temperature (Po)	Control	Treated
98–99 (F)	4	12
99–100	15	17
100–101	16	7
101–102	8	6
102–103	6	7
103–104	1	
104–105		1
Total	50	50

exhibited by the patients in each group. The vast majority of patients in both groups had some fever after surgery and there was not a striking difference between the two groups (table 14). When the highest postoperative temperatures exhibited by the patients in each group were compared, no significant difference was established. The average in the control group was 100.7F with a standard deviation of 1.3 degrees and in the treated group the average was 100.4F with a standard deviation of 1.5 degrees.

6) Postoperative days in the hospital. The control and treated groups were compared in regard to the length of time, postoperatively, the patients had stayed in the hospital. In this comparison only patients with single resections were used and four of these patients (two in each group) were omitted because of prolonged hospital stays due to the following complications: neurogenic bladder, cerebral vascular accident, myocardial infarction, and extravasation of urine into the tissues. The average postoperative hospital stay of the 20 patients with single resections in the treated group was 11 days. The standard deviation was 5.7 days. The average postoperative stay in the 19 patients with single resections in the control group was 14 days. The standard deviation was 7.2 days. Thus there was not a significant difference in the two groups between the length of stay in the hospital after the operation.

7) Mortality. There was one death in each group. One patient with valvular heart disease developed acute bacterial endocarditis due to M. pyogenes and the other died of acute heart failure on the forty-third postoperative day. It is of interest that in the former case the organism was able to become implanted on the heart valve in spite of the chloramphenicol.

8) Toxicity. All of the patients in the group who received chloramphenicol were tested repeatedly for evidence of depression of the bone marrow. In no instance was this toxic effect noted even in the patients who received chloramphenicol for up to 23 days. The drug was well tolerated in each case and no evidence of either upper gastrointestinal upset or of diarrhea was found.

DISCUSSION

Taken as a whole, the results of this study did not appear to indicate any marked differences between the group of patients given chloramphenicol before and after the surgical period and the group of patients who were not given this medication. The total daily dose of the drug was somewhat lower than we have used therapeutically and this may partly explain why its administration had no demonstrable effect on the postoperative urine cultures (table 12). We do not interpret these data as showing that chloramphenicol is harmful when given on a prophylactic basis but believe that the point of emphasis should be that we failed to demonstrate any advantage to its use in this prophylactic manner. There does not appear to be any valid objection to the use of prophylactic antibiotics for patients with valvular heart disease and with other conditions that may make them particularly susceptible to a transient bacteremia. On the other hand, we were unable to find in this alternated group of patients any advantage to the use of prophylactic chemotherapy. Furthermore, the fatality in this series due to an acute endocarditis should emphasize that prophylactic chemotherapy will not invariably give protection. It must be admitted that the objections to the use of prophylactic chemotherapy are, for the most part, theoretical[1, 3] and are based on experiences with M. pyogenes and with patients with tracheotomies.[7] It is still to be shown that usage of antimicrobial agents have specifically caused changes in the sensitivity of most gram-negative bacilli to the wide spectrum antibiotics. Recent studies in our laboratory and by others suggest, however, that such a change may now be taking place.[17] Furthermore, there is a definite risk to the patient when any medication is given and antibiotics have proved no exception to this rule.[4] Therefore, before one is justified in administering antibiotics on a routine basis in any condition, it should be definitely established that this routine administration will be to the patients' advantage. We feel that in regard to the prophylactic use of antibiotics in transurethral resection of the prostate gland this criterion as yet has not been met. On the other hand, in those patients in whom an indication that valvular heart disease, severe urinary tract infection or extreme debilitation exists there do not appear to be many valid objections. It is not unreasonable to assume that the prophylactic therapy in these particular groups of patients may be more effective if it is not used indiscriminately in less seriously ill or less complicated patients.

SUMMARY AND CONCLUSIONS

In order to study the effect of routine prophylactic antimicrobial therapy upon the results of transurethral resection of the prostate gland, chloramphenicol was given in strict alternation to fifty of one hundred consecutive cases. No significant effect on the immediate postoperative complications, postoperative bacteremia, postoperative urine cultures, postoperative drainage period, postoperative pyrexia, postoperative hospital stay or mortality was demonstrated. The medication was tolerated well and no toxicity was noted. This study did not provide evidence to justify the prophylactic use of antibiotics in transurethral resection of the prostate. Until such evidence is forthcoming, it is questionable whether such usage is justified.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

PROSTATIC ADENOCARCINOMA COMPLICATED BY THE DEVELOPMENT OF EPIDERMOID CARCINOMA OF THE URETHRA: REPORT OF TWO CASES

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Prostatic adenocarcinoma is fairly common in older men while carcinoma of the urethra is comparatively rare. Since both neoplasms have their greatest incidence during the latter decades of life, it is conceivable that they should occur simultaneously. However a survey of the literature has failed to uncover any reports of such a coexistence. We have studied 2 cases in which prostatic adenocarcinoma was complicated by the development of epidermoid carcinoma of the prostatic urethra. In neither case was the second tumor suspected during life and was demonstrable only after postmortem examination by microscopic study of the affected tissues.

CASE REPORTS

Case 1. A 60-year-old white man was admitted to another hospital in June 1950 with symptoms typical of obstructive and inflammatory uropathy. The admission studies demonstrated a hard, enlarged prostate and an infection of the urinary tract. Serum acid and alkaline phosphatases were normal; x-ray studies revealed no evidence of bony metastases.

Transurethral resection of the prostate was performed in July 1950. Tissue examination showed that, in many of the fragments, the fibromuscular stroma and glands were replaced by diffusely growing and invading carcinoma cells arranged in a glandular pattern. These small glands were closely packed together. The individual cells showed only moderate variation in size and shape. The nuclei were generally large, having regularly distributed chromatin and rather prominent nucleoli; occasional mitoses were observed. There were considerable numbers of eosinophils scattered throughout the carcinoma. A diagnosis of prostatic adenocarcinoma was made.

Twelve days later, bilateral orchiectomy was performed. Medication with 5 mg. daily of stilbestrol was initiated and maintained continuously.

The patient was readmitted to the same hospital in February 1951 with recurrence of the obstructive urinary tract symptoms and evidence of cardiac decompensation. He was digitalized, and a secondary transurethral resection of the prostate was performed in March 1951. Microscopic study demonstrated prostatic adenocarcinoma, grade 2. No signs of regressive changes were seen. Despite endocrine medications, the patient did not improve.

He was admitted to this hospital in September 1951 in a terminal condition. He suffered from persistent vomiting and severe back pain. Apart from the administration of 30 mg. daily of stilbestrol, treatment was symptomatic only.

Accepted for publication June 14, 1955.

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He died about one month after admission and 16 months after the institution of androgen control measures An autopsy was performed

Gross autopsy findings Pertinent findings were restricted to the genitourinary system No evidence of primary carcinoma was detected elsewhere

The prostate, the neck of the bladder and the seminal vesicles were fused together into one firm mass by infiltrating tumor tissue This mass was adherent to the right iliac bone, which was directly invaded by tumor tissue

The prostate was slightly enlarged and was composed of hard, greyish-white tissue The bladder wall was thickened and its posterior portion was infiltrated by tumor On the posterior wall of the prostatic urethra, there was a small area of mucosal thickening and roughening There was gross evidence of acute and chronic cystitis Both the ureters and the renal pelves were dilated and, on the right side, were filled with pus The kidneys showed acute and chronic pyelonephritis Both testicles were surgically absent

Microscopic The prostate was infiltrated by two distinct types of neoplasm, adenocarcinoma and squamous cell carcinoma (fig 1, *A*) These two varieties did not blend into one another and invaded independently

The adenocarcinoma was composed, for the most part, of relatively small rounded cells with central nuclei and small amounts of lavender-colored cytoplasm In many areas, the cells were arranged in large clusters and exhibited some tendency to form small acini In a few areas, the cells aggregated in broad bands and showed no glandular characteristics The squamous cell carcinoma was fairly well differentiated and individual cell keratinization and intercellular cytoplasmic bridges could be detected in a number of areas Invasion of perineural lymphatics by the adenocarcinoma was seen A few prostatic glands and ducts could be identified and these exhibited squamous metaplasia The metaplastic cells had small central nuclei and large amounts of pale or clear cytoplasm

Arising in the *prostatic urethra* was a squamous cell carcinoma (fig 1, *B*) The invasive neoplasm originated from multiple foci, which were separated from one another by small strips of mucosa showing intraepithelial epidermoid carcinoma The neoplasm spread into the adjacent prostate and bladder wall The carcinoma was well differentiated

The mucosa of the bladder and the prostatic urethra exhibited patchy squamous metaplasia There was also a moderately severe acute and chronic inflammation with multiple areas of ulceration

The posterior wall of the bladder was infiltrated by both adenocarcinoma and squamous cell carcinoma The two varieties remained distinct from one another

Autopsy diagnosis Adenocarcinoma of the prostate with invasion of the bladder squamous cell carcinoma of the prostatic urethra with invasion of the prostate and the bladder, squamous metaplasia of the mucosa of the bladder and the urethra and of prostatic glands and ducts, surgical absence of both testicles, acute and chronic ulcerative cystitis and urethritis and bilateral acute and chronic pyelonephritis

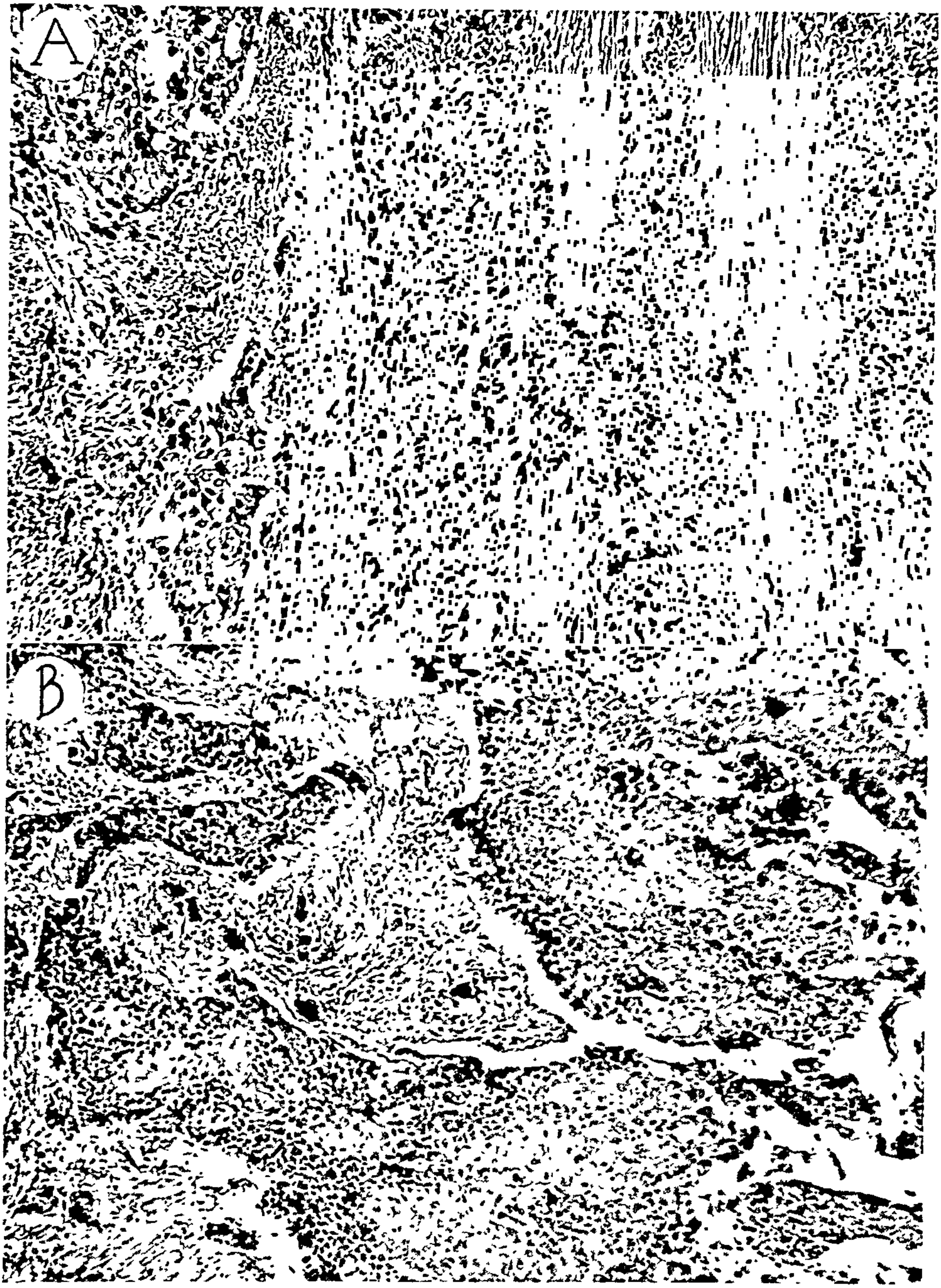

FIG. 1. Case 1. *A*, undifferentiated adenocarcinoma and squamous cell carcinoma infiltrating prostate. *B*, squamous cell carcinoma arising in mucosa of prostatic urethra.

Case 2. A 60-year-old Negro was admitted to another hospital in May 1952 with typical symptoms of obstructive uropathy. Examination revealed a nodular, hard, enlarged prostate, suggestive of carcinoma. Radiologic studies demonstrated no evidence of bony metastases. The serum acid phosphatase was slightly elevated and the serum alkaline phosphatase was normal.

Transurethral resection of the prostate was performed in June 1952. Microscopic study of the specimen showed the presence of adenocarcinoma of the prostate The tissue was extensively infiltrated with tumor consisting of small cells forming no particular pattern The cells were uniform in size, shape and staining reaction and generally oval or round In a few areas there was an attempt at acinar formation There was considerable edema of the tissue The benign prostatic glands were not remarkable Five days later, bilateral orchiectomy was performed Stilbestrol medication, 5 mg daily, was instituted and the patient was discharged

During the ensuing 22 months the patient obtained a moderate amount of relief of his obstructive urinary symptoms He was followed at home by his private physician During this time he experienced some cardiac decompensation and was digitalized

He was admitted to this hospital in March 1954 with a complaint of pain in the right lumbar area extending down the back of his right leg The pain was said to have developed several weeks before this admission following his stumbling after lifting a heavy object The patient stated that he had been taking a stilbestrol preparation, 5 mg daily, ever since his operation in 1952 He had no abnormal urinary symptoms except nocturia Admission examination revealed a prostate which was hard, irregular, fixed and clinically malignant There was moderate limitation of forward flexion of the back associated with tenderness over L-5 and L-4 interspaces on the right Laboratory studies demonstrated normal acid and alkaline phosphatase levels X-rays of the lumbosacral spine and pelvis revealed no evidence of metastases

Shortly after admission, the patient had swelling and pain of the entire right lower extremity which was considered to be due to a venous occlusion A prolonged course of anticoagulants was given and there was gradual improvement However, he continued to complain of pain in the right sacroiliac and right lumbar areas which radiated down along the right sciatic nerve distribution In June, x-ray studies of the lumbosacral spine demonstrated that the superior articular facet and the right transverse process of L-5 and the inferior articular facet of L 4 on the right had been destroyed by an osteolytic process (fig 2) The patient's pain became progressively worse and a chordotomy was performed in September 1954 Estrogen medication was maintained throughout his hospitalization His condition continued to deteriorate, and he expired in November 1954, 29 months after the initiation of androgen control measures An autopsy was performed

Gross autopsy findings External examination showed an emaciated, elderly colored man with multiple decubitus ulcers The right lower extremity was moderately edematous

The prostate, the seminal vesicles and the neck of the bladder were infiltrated by tumor fusing them together forming a hard nodular mass Tumor tissue had infiltrated into the posterior wall of the bladder and in a few areas had penetrated into the mucosa The renal pelves, the ureters, the bladder and the urethra contained purulent material Both ureters and both renal pelves were slightly dilated and there was bilateral acute and chronic pyelonephritis The

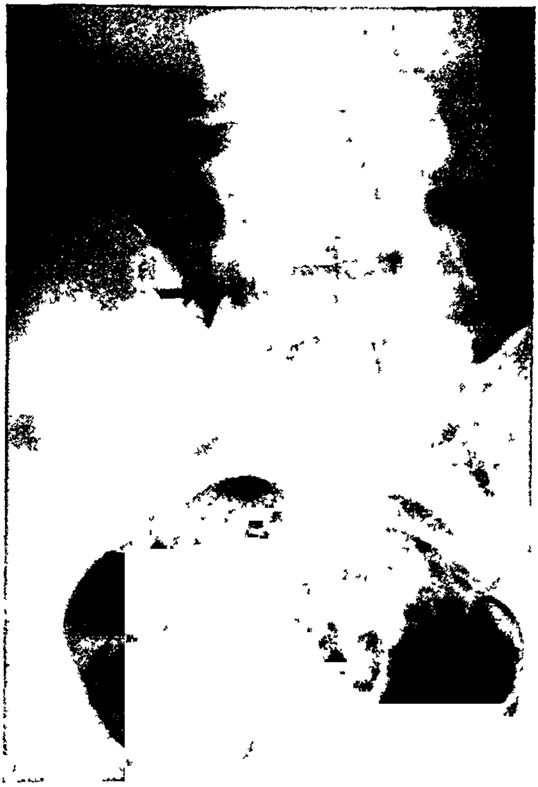

FIG. 2. Case 2. X-ray showing erosion of right transverse process and right superior articular facet of L-5 and of right inferior articular facet of L-4.

mucosa of the bladder and the prostatic urethra was granular and hyperemic with spotty areas of ulceration.

The iliac, sacral, lumbar and para-aortic lymph nodes contained metastatic carcinoma and were matted together forming a large mass, which had compressed the right iliac vessels. In the center of this conglomeration of lymph nodes, necrosis and abscess formation had occurred. Tumor had extended from the nodes into the sacrum and the lower lumbar vertebrae.

Pertinent changes were not encountered elsewhere. There was no evidence of primary carcinoma in any organ other than the prostate.

Microscopic studies: The prostate was extensively infiltrated by adenocarcinoma and to a lesser extent by squamous cell carcinoma (fig. 3). The adenocarcinoma exhibited a fairly marked tendency to form small glands. These neoplastic cells were cuboidal with round central nuclei and moderate amounts of slightly foamy eosinophilic cytoplasm. The epidermoid carcinoma spread into the deeper portions of the prostate, maintaining its distinctness from the adenocarcinoma. The squamous cell carcinoma was characterized by ample amounts of cytoplasm, either slightly eosinophilic or clear. In numerous areas, keratinization was seen. This neoplasm invaded perineural lymphatics.

The lymph nodes containing metastatic carcinoma were extensively necrotic, but multiple nests of metastatic epidermoid carcinoma could be detected.

In the sacrum and the lumbar vertebrae, the metastatic carcinoma was ex-

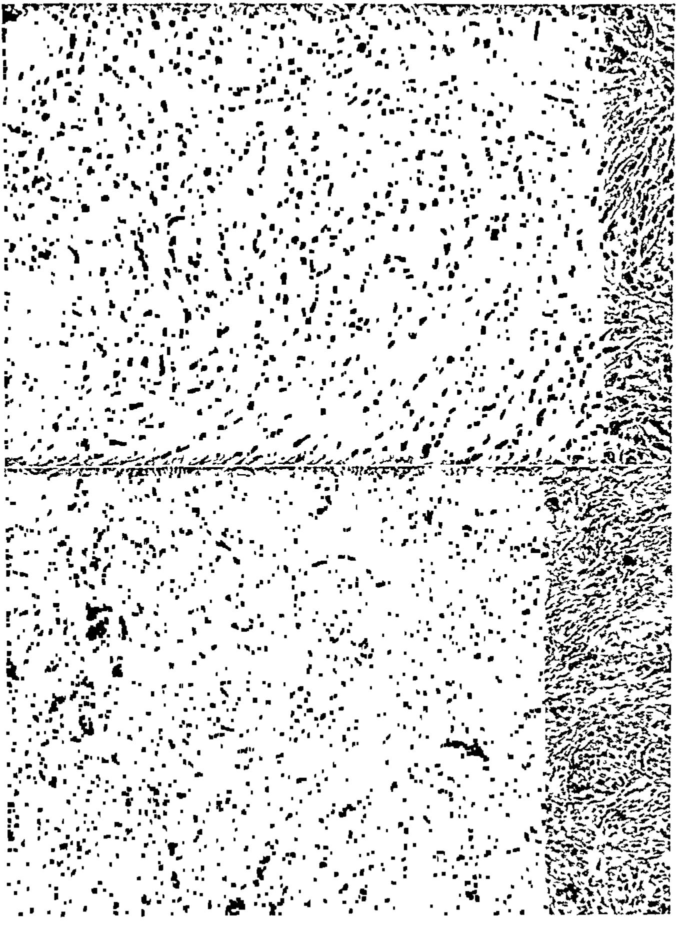

FIG. 3 Case 2. *A*, prostatic carcinoma. *B*, squamous cell carcinoma infiltrating prostate.

clusively squamous in type (fig. 4). It had produced erosion of the invaded bone. Extensive necrosis of the neoplasm in these sites had occurred.

The mucosa of the bladder and the urethra had undergone patchy squamous metaplasia, and this change was associated with severe acute and chronic ulcerative inflammation. In the urethra several foci of atypical squamous metaplasia were seen. In these areas there were proliferation of the basal cells, loss of cellular polarity and occasional mitotic figures. No invasion of the subepithelium by

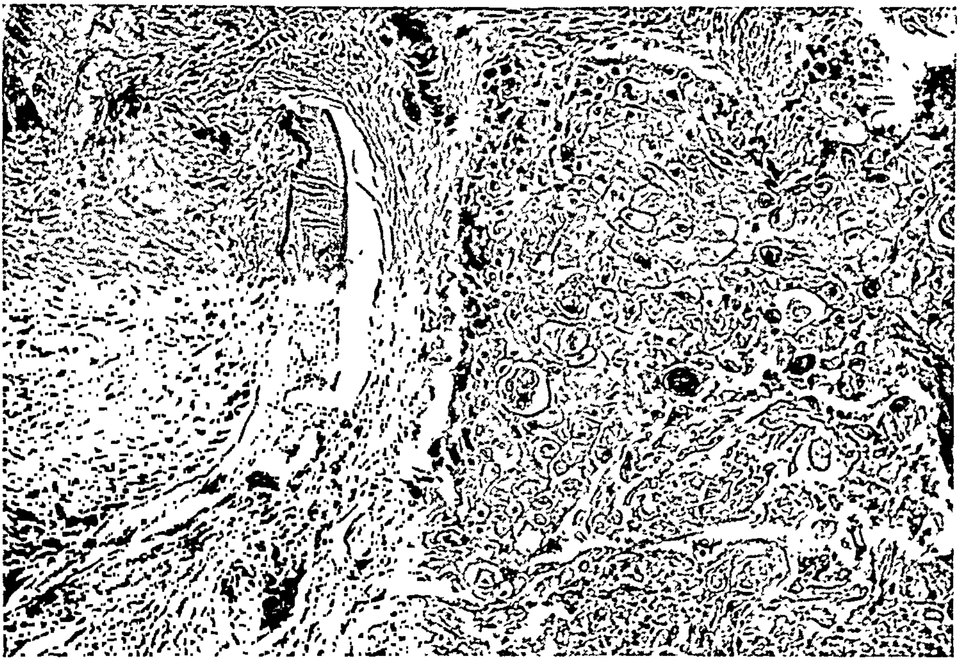

FIG. 4. Case 2. Metastatic squamous cell carcinoma in vertebral column. Note spicule of bone to left of center of field.

these atypical cells could be detected. The posterior wall of the bladder was fairly extensively infiltrated by carcinoma, almost entirely glandular in type.

Autopsy diagnosis: Adenocarcinoma of the prostate with invasion of the bladder; squamous cell carcinoma, probably arising in the prostatic urethra, with invasion of the prostate and the bladder and with metastasis to the regional lymph nodes and to lumbar vertebrae; squamous metaplasia of the mucosa of the bladder and of the urethra; surgical absence of both testicles; acute and chronic ulcerative cystitis and urethritis and bilateral acute and chronic pyelonephritis.

DISCUSSION

We have described 2 cases in which adenocarcinoma of the prostate was complicated by the development of epidermoid carcinoma of the urethra. Inasmuch as epidermoid carcinoma was not seen in tissue removed by transurethral resection in either case, we believe that the urethral tumors developed later than the prostatic adenocarcinomas. Further, the clinical aspects do not suggest the presence of urethral carcinoma throughout the course of the disease. In both instances, the urethral tumor invaded the prostate and was first suspected when epidermoid carcinoma was encountered in coexistence with adenocarcinoma in routine sections prepared from the prostate. More detailed studies demonstrated that no blending occurred between the two varieties of neoplasm. In the first case, a review of the gross tissues demonstrated a small area of roughening in the mucosa of the prostatic urethra and microscopic study disclosed that an epidermoid carcinoma had arisen in that area. In the second case, the exact site of origin could not be detected despite a fairly intensive search in the bladder, the vesical neck and the prostatic urethra. However squamous metaplasia of much of the mucosa with foci of atypical cells was observed in the prostatic urethra and it is believed that the neoplasm probably arose from a minute focus which could not be discovered. Both Dixon and Moore and Thompson, Albers and Broders believe that squamous cell carcinoma encountered in the prostate most probably has its origin in the prostatic urethra. Thompson and his associates were apparently unable to detect the suspected origin in the urethra in 7 cases, which they therefore classified as "squamous cell carcinoma apparently arising primarily in the prostate".

Osteolytic metastases are produced rather uncommonly by primary carcinomas of the prostate while osteoblastic lesions are considered to characterize the disease. Elkin and Mueller reported that, in 61 cases with bone metastases, only 13 per cent of the secondary lesions were purely lytic and 23 per cent mixed sclerotic and lytic. These workers did not correlate the histologic structure of the tumor, primary or secondary, with the radiologic appearance, but only one of their cases apparently contained epidermoid elements in the prostatic tumor. In our second case and in one of the 7 cases of squamous cell prostatic carcinomas (probably primary urethral neoplasms) described by Thompson and co-workers, osteolytic lesions were produced. Radiologic studies were not made in our first case. Such bone lesions, when encountered in proven cases of adenocarcinoma of the prostate, may suggest the possible superimposition of squamous cell carcinoma of the urethra.

We have encountered these two examples of the coexistence of prostatic and urethral neoplasms in a series of 14 autopsies performed on cases of overt prostatic carcinoma during a 3-year period. This suggests that this association may not be too uncommon but, as previously mentioned, a survey of the literature indicates extreme rarity. We believe that others may have encountered instances of this condition, but may not have recognized them. The epidermoid carcinoma in the prostate may have been confused with benign metaplasia, with metaplasia of the prostatic adenocarcinoma or with primary squamous cell carcinoma of the prostate. Much emphasis has been laid upon the fact that squamous metaplasia of prostatic epithelium occurs fairly frequently and that this change must not be mistaken for epidermoid carcinoma. Perhaps the reverse may occur and epidermoid carcinoma may be considered to be benign metaplasia. Squamous metaplasia of prostatic adenocarcinoma occurs rarely, though it might be expected to be common in view of the propensity of its parent epithelium for this change. To justify a diagnosis of epidermoid metaplasia of adenocarcinoma, intimate admixing and blending of the two types of carcinoma should be found. Primary epidermoid carcinoma of the prostate is a rare tumor and to substantiate such a diagnosis squamous cell carcinoma of the urethra must be conclusively excluded. With the exception of a case described by Walthard and of another by Elkin and Mueller prostatic epidermoid carcinoma has apparently not been associated with a glandular tumor of that organ.

It is interesting to speculate whether or not the complicating of prostatic adenocarcinoma by urethral epidermoid carcinoma is merely fortuitous. It must be recalled that both these cases were subjected to transurethral resection and to prolonged androgen-control measures. There appears to be a definite association between urethral irritation and the development of carcinomas in that tissue. It is conceivable that the resections together with infection may have provided the necessary stimulus. On the other hand, it is well recognized that the administration of stilbestrol leads to squamous metaplasia of the epithelium of the prostate, the utricle and the urethra. In both of our cases, metaplasia was seen in these sites. The relationship between squamous metaplasia and the development of carcinoma of the bladder is an unsettled problem. As the mucosa of the prostatic urethra is similar to that of the bladder, it is felt that the significance of squamous metaplasia of the urethra in relation to the evolution of epidermoid carcinoma cannot be evaluated at this time. The possible role of stilbestrol as a direct carcinogenic agent or as a potentiator of another unknown agent must be considered. It has been shown in certain susceptible strains of experimental animals that stilbestrol will produce neoplasms of the bladder and of the renal tubules. Hueper, in his extensive review of environmental cancer, suggests that some individuals may be particularly susceptible to the cancerogenic action of estrogenic substances, and that it may be that such substances may induce tumors of the kidney and the bladder in man as well as in experimental animals. However, these speculations though interesting have no firm basis and pure coincidence may account for the coexistence of the prostatic and urethral neoplasms.

SUMMARY

Two cases of prostatic adenocarcinoma complicated by the development of epidermoid carcinoma of the prostatic urethra have been described. Both cases were subjected to transurethral resections and to androgen-control measures. The urethral neoplasms were not suspected until epidermoid carcinoma was encountered in routine sections prepared from the prostate after postmortem examination. In one case, the squamous cell carcinoma metastasized to the vertebral column producing an osteolytic lesion.

A review of the literature has not revealed other reports describing this association of prostatic and urethral neoplasms.

The cases are discussed briefly and a few speculations concerning the significance of the coexistence of the tumors are entertained.

Photographs were prepared by R. M. Christopher and R. D. MacIntyre, Medical Illustration Laboratory, Veterans Administration Center, Temple, Texas.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

THE LIPIDS IN THE PROSTATE GLAND OF THE DOG

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Much confusion exists in the literature as to the lipid components of the dog prostate and their role in the prostatic secretion; thus a systematic review of the lipid cytochemistry was undertaken as a preliminary study for further planned investigations.

This study deals with the localization and identification of lipid components of normal prostatic tissue and secretion in the dog throughout the various phases of the secretory cycle.

It is also hoped that this investigation may serve as a basis for wider use of the dog as a study and experimental animal in prostatic investigations.

HISTORICAL BACKGROUND

Due to ease of staining, the lipids were the first group of identifiable substances explored. Despite this, much confusion exists over the identification and localization of lipids within the prostatic epithelium and secretion throughout the secretory cycle.

In 1873 Thompson first described fat droplets in the prostatic cells of man. Confirmatory evidence on the presence of lipids in human prostatic cells was supplied by Posner and Scheffer ('09) and by Plenge ('24). The sudanophilia and birefringency of prostatic lipids in man and dog at various ages and pathological states were further investigated by Kinoshita ('20). In addition, Kunze ('22) described the physiological significance of the morphologically demonstrable lipids in the prostate of the dog and various other mammals. Basal infranuclear fat droplets have been described by Gylling ('41) in the prostate of the castrated rabbit. Of particular histochemical interest is the work of Pretl ('48) on the lipid and lipo-protein complexes and their metabolism in the human prostate.

MATERIALS AND METHODS

Twenty mature male dogs of various ages and breeds were used in this study. The animals were anesthetized with sodium diethyl-barbiturate and killed by injections of air.*

For general topographical and cytological study, sections (5u) were made of tissues fixed by immersion in the fluids of Bouin, Zenker, Rossman, absolute alcohol, and of Van de Grift. A number of staining methods were employed: Masson's trichrome Maximov's eosin-azure method, Azan, Mallory's connective tissue stain, hematoxylin and eosin, and iron hematoxylin.

In addition, adjacent portions of the prostate were rapidly removed and di-

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Accepted for publication September 21, 1955.
This work was partially supported by a Public Health Grant (C-2493).

* These animals were obtained through the courtesy of the Department of Pharmacology, Emory University, Georgia.

rectly frozen in isopentane at approximately −150°C and later dehydrated *in vacuo* at −45°C for about 48 hours When dry, the blocks of tissue were infiltrated with paraffin (52°–53°) in vacuo for 15 minutes and embedded Sections 5u thick were mounted on slides with slight pressure without the use of an albumen fixative The paraffin was removed by immersion in two changes of petroleum ether Before staining, the sections were denatured in absolute alcohol for 12–18 hours Whenever possible, these frozen dried sections were always compared with those sections fixed by the more commonly used histological techniques

Lipids were studied in freshly frozen sections (10–15u) fixed in 10 per cent neutral formalin, neutral buffered formaldehyde (Lillie '48), formal-calcium (Baker '46) formal calcium-cobalt (Baker '46) and weak Bouin's fluid (Baker '46) The total lipid and neutral fat content was visualized by the following staining procedures Sudan Black B, Sudan III (Herxheimer's '04 mixture), Fettrot (Ciba), Oil Red O, Oil Blue N (Lillie '44) and Nile Blue Sulphate (Lison '36, Cain '47) For the demonstration and identification of the phospholipids, the acid-hematein method of Baker ('46) followed by the pyridine extraction procedure, and the performic acid Schiff method (PFAS), (Pearse '51), was used The presence of metachromatic phosphatides was established by the use of Feyrter's ('36) tartaric acid thionin mixture For the study of cholesterol and its esters, the Liebermann-Burchardt reaction, Schultz method, (Romeiu '27 modification) and digitonin reaction (Lison '36) and subsequent staining with Sudan 3 were employed Unstained frozen sections sectioned at 10–12u were observed, both in a dark field and in polarized light for birefringence

In addition, an analysis of the lipids by the paper chromatography method of Hack '53 was also used

GENERAL MORPHOLOGY

The mature prostate gland in the dog is a compact musculoglandular organ whose terminal apocrine secretory elements consist of tubuloalveolar glands (Walker, 1899, Stieve, '30) No difference in structure or function could be ascertained in the dorsal or ventral segments of the dog prostate, although such differences were noted by Zuckerman and Groome ('37), and Arcadi ('52) Furthermore, it is of physiological and histochemical advantage to use this animal for both the seminal vesicles and bulbourethral glands are absent in the dog, thus, one can easily study the mode of secretion and the prostatic secretion itself without fear of any contamination

Grossly, the alveoli (figs 1, *A*, 2, *A*, 5, *A*) are relatively large, saccular structures, which have a diameter of about 0 15 mm , and occupy the greater part of the lobule Distention of the alveoli to two or three times its normal size occurs normally at the period of maximum secretory activity, or under the stimulation of cholinergic drugs in the dog, as has been reported by numerous investigators

Microscopically, the secretory acini are lined with a simple stratified or pseudostratified tall columnar epithelium (figs 1, *A*, 5, *A*), resting on a discontinuous basal layer of flattened or cuboidal cells Consequently, in any given section

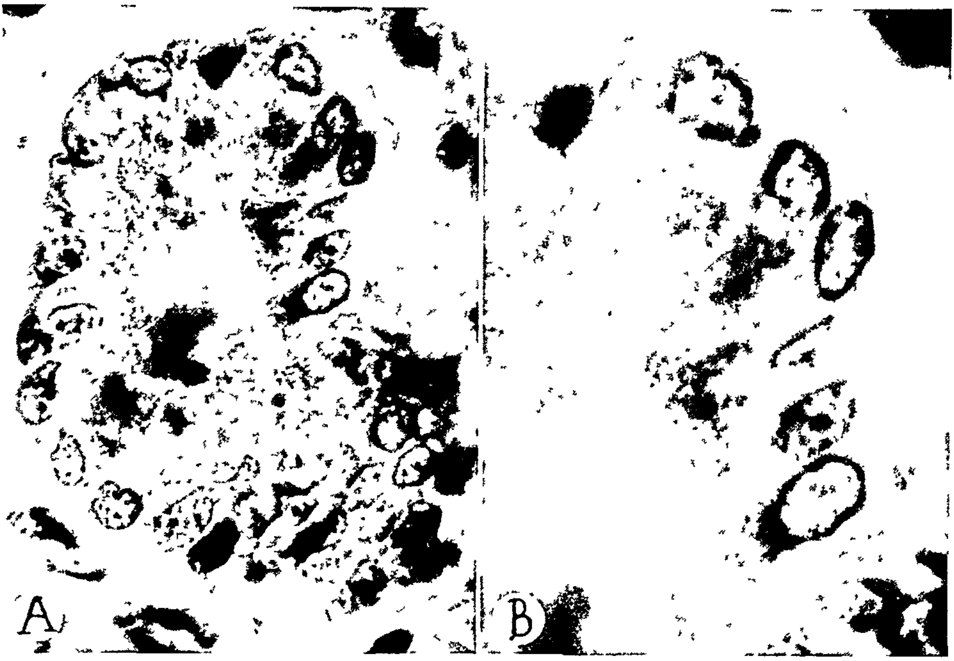

FIG. 1. *A*, an active secretory acinus may be lined with tall, simple columnar epithelial cells. Distal cytoplasm is filled with numerous discrete secretory granules Note flocculent nature of secretion in acinar lumen. Fixation: Zenker-formol. Masson's trichrome stain. ×1400. *B*, distal surface of cells at time of secretory discharge presents ragged appearance. Note that some secretory granules have been discharged into lumen. Fixation Zenker-formol: Masson's trichrome stain. ×2780

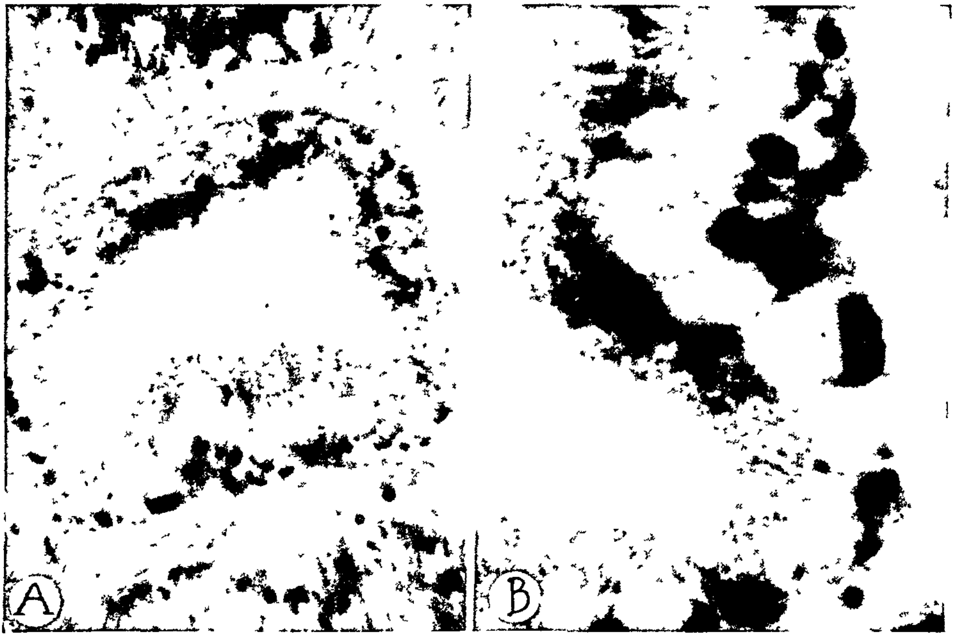

FIG. 2. *A*, localization of neutral fat and phospholipids in secretory epithelium. Fine bodies in distal cytoplasm are mitochondria. Fixation: 10 per cent neutral formalin, frozen section. Sudan Black B. ×1150 *B*, distal cytoplasm with its very fine bodies displays a lighter, but positive sudanophilia. These cells are actively discharging their secretion; note the ragged distal surfaces of the cells Fixation 10 per cent formalin containing 1 per cent calcium chloride, frozen sections. Sudan Black B. ×2780.

there may be several strata of nuclei; hence, giving it the stratified or pseudostratified appearance so commonly ascribed to it. The basally located cells possess a small, rather dense elliptical nucleus, whose long axis is perpendicular to the acinar wall. Arcadi ('52) reports that these "peculiar granular cells" contain a glycogen-protein complex.

Due to the limitation of space within a single acinus, and the cells, the gland cells may assume various forms: pear-shaped, polygonal or triangular (Walker, 1899). The tall, active, secretory cells (figs. 2, *B;* 5, *A*) are further characterized by a large amount of dense cytoplasm, fully charged with rather large acidophilic granules in the apical portion. The large (7u) moderately chromatic nucleus is situated in the basal part of the cell, and displays two shapes: elliptical, if a remnant of the luminal cell wall is present: and round, when the cell membrane has ruptured.

Dependent upon the stage of the secretory cycle, the free cell surfaces of the tall, columnar epithelium present several aspects. At the time of secretory discharge, the luminal surface presents a ragged or uneven appearance (fig. 2, *A* and *B*), as if the cell membrane were ruptured with the result that the cytoplasm with its secretory inclusions are confluent with the secretion within the lumen. Moore ('36) has already suggested that the mode of prostatic secretion in man is of an apocrine nature, and possibly this also holds for the dog. In other cells, just approaching full secretory activity, the distal cell membrane is smooth, intact, but bulges into the acinar lumen, forming tongue-like projections (Stieve '30), filled with secretory materials (figs. 1, *A* and *B* and 5, *A*). In inactive cells, the distal cell membrane is intact and well-defined.

The prostatic secretion within the acini in the dog is of a flocculent nature (figs. 1, *A* and 5, *A*), containing a few cellular elements such as shed epithelial cells and lymphocytes. No corpora amalycea have been observed in this study, although Zuckerman and McKeown ('38) have reported their presence in dogs. Leydig (1850) describes prostatic stones but his accompanying figure shows it to be also a flocculent fluid.

LIPIDS AND LIPOPROTEINS

The neutral fat content of prostatic cells in the mature dog was visualized by the use of Sudan III (Herxheimer's mixture '04), the supersaturated isopropanol technique of Lillie ('44) with Oil Red O and Oil Blue N, a saturated solution of Fettrot (Ciba)*, and Sudan Black B (Baker '46) In this study, neutral fat stained by the above named fat colorant dyes such as Sudan III, Oil Blue N, Oil Red O, and Fettrot, showed that the greater mass of neutral fat was confined to an infranuclear position (fig. 2) in the form of several rather large distinct droplets (Kinoshita '20, Kunze '22, Arcadi '52, and others). These fat droplets may also coalesce to form a single large infranuclear mass (figs. 2, *A* and *B* and 3, *A*).

Further examination revealed that there are also present few small droplets of neutral fat located in a juxtanuclear (Kinoshita '20) and in a supranuclear

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* A sample lot of this dye was supplied through the courtesy of Ciba Co., 627 Greenwich St., New York 14, N. Y.

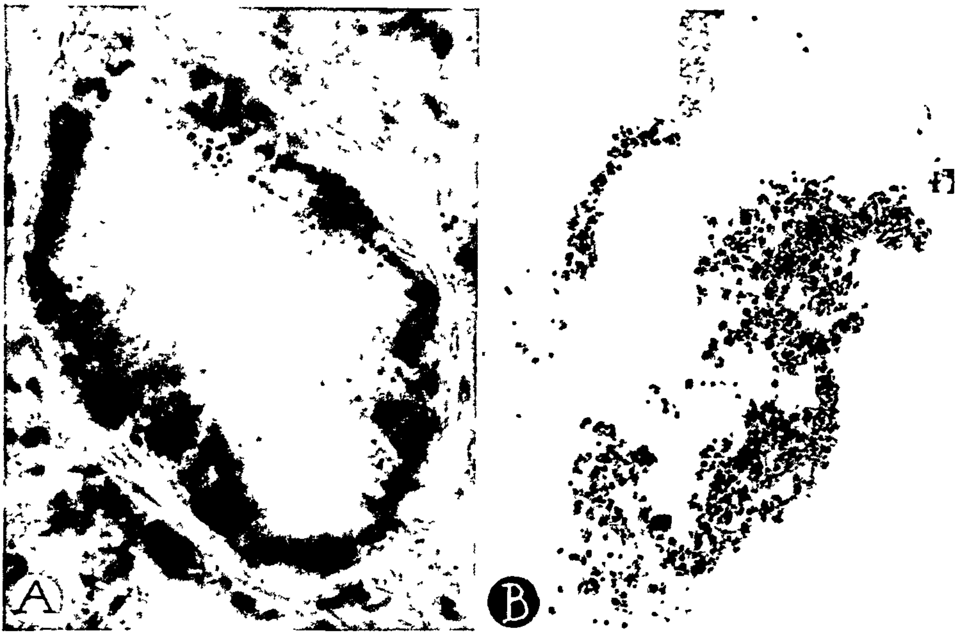

FIG. 3. *A*, localization and migration of neutral fat in acinar epithelial cells. Neutral fat is seen passing into acinar lumen. Fixation: 10 per cent neutral formalin. Oil red O. ×1400. *B*, foci of birefringent lipids contained both in prostatic epithelium and stroma are common. Birefringent lipids seem to mainly correspond to localization of neutral fat bodies. Unstained and examined with polarized light. Fixation· 10 per cent neutral formalin. ×2775.

position (figs. 2, *A* and 3, *A*), where they probably pass into the lumen. Neutral fat droplets can be frequently observed in the fluid contained in a prostatic acinus (Posner and Rapoport '05, Posner and Scheffer '09, Plenge '24, and others). This suggests perhaps that there is a continual fat migration from the large basal mass of neutral fat to the lumen of prostatic acini. However, Kinoshita '20 denied the migration of neutral fat and further added that these fat droplets did not seem to be clearly connected with any secretory stage. In the dog, the so-called basal lipoid cell Kinoshita ('20) saw in man was absent.

With Sudan Black B staining, the distribution and volume occupied by the lipids were greater (fig. 2, *A* and *B*) than that demonstrated by the fat colorant methods. In addition, the distal cytoplasm with its very fine inclusion bodies displays a lighter, but still a distinct positive sudanophilia. This increase in lipid staining can be explained by the fact that Sudan Black B is known to also stain both neutral fat and phospholipids. Comparison with slides prepared and stained with anilin acid fuchsin methyl green method of Bensley ('38), and the methyl green modification of Altmann's technique by Gabe ('47), reveals that some of these small rod and spherical-shaped bodies in the cytoplasm probably are mitochondria (fig. 5, *A*). These small phosphatide-containing bodies which are probably mitochondria were also observed by Policard and Noel ('20).

In a single prostatic lobule, the distribution of neutral fat is "patchy" and characterizes only those acini which are actively secreting or approaching maximal secretory activity. The remaining ones display only very fine droplets of

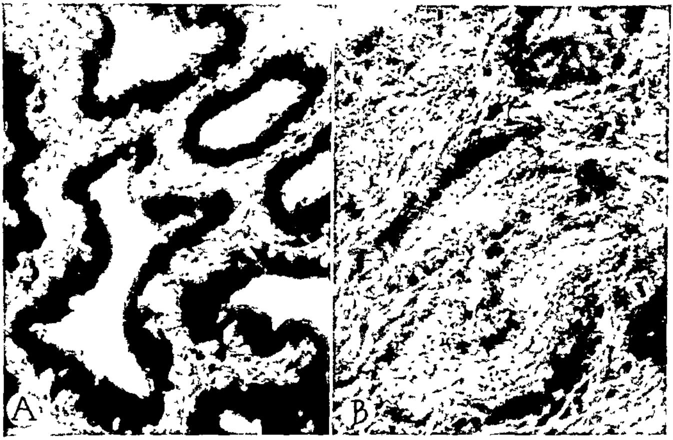

FIG. 4. *A*, localization of phospholipids in distal secretory portion of prostatic cell. Some of positive material is phospholipids associated with mitochondria. Fixation: formaldehyde-calcium, frozen sections. Baker's '46 acid-haematein test. ×1156. *B*, this preparation was subjected to Baker's control procedure, extraction with pyridine, exhibited no positive staining of materials in acinar cells; thus confirming presence of ester phosphatides. Nuclear substance always gives a positive reaction. Fixation: Formaldehyde-calcium, frozen sections. Baker's '46 acid-haematein test, with pyridine extraction. ×1156.

fat dispersed throughout the cytoplasm. Very fine discrete bodies of neutral fat were observed in the underlying and interacinar connective tissue. As has been frequently observed in man (Schlagenhaufer '09, Kawamura '11, Kinoshita '20, Swyer '42, and others), the deposition of fat in the dog also increases with age and in glandular hyperplasia (Kinoshita '20, Zuckerman and McKeown '38).

With the Baker's acid-haematein a heavy positive reaction (blue-black in color) was seen concentrated in the distal portion of an actively secreting cell (fig. 4, *A*). The prostatic secretion contained in the lumen of the alveoli was unstained. This positive material, according to Baker '46, is a phospholipid; that is a lecithin, cephalin, or a sphingomyelin. In order to distinguish between the phospholipids and other nonlipid substance giving a positive reaction, preparations were subjected to Baker's control procedures, consisting of extracting the material with pyridine previous to staining. These preparations exhibited no positive staining of the acinar cells (fig. 4, *B*), or the prostatic secretion. However, the nuclear substance in the cells and in the secretion in the lumen were stained, a feature characteristic of Baker's control test. This phenomenon suggests perhaps that the lecithin was decomposed during the secretory process and split into an organic phosphate and choline. Lundquist ('46) found evidence for this postulation in biochemical work on human semen. Scott ('45) demonstrated lecithin in a biochemical assay of the human prostatic gland itself, but not in the fluid. Farrell ('31) in his biochemical assay of dog prostatic secretion failed to corroborate the presence of lecithin.

An attempt was made to further separate and identify these phospho using the paper chromatography of Hack ('53), but this means of lipid an yielded no further information to the phospholipids, or the other lipids cont in the prostate.

Further evidence on the presence of lecithin in the prostatic epitheliun revealed by the use of a 1 per cent Nile Blue sulphate solution (Lison '36) the Nile Blue method of Cain ('47). A diffuse but strong positive blue colo found in the prostatic epithelium as demonstrated by Lison ('36), in whicl lipids will dissolve the osazone and combine with the free base to form blue soluble compounds. It was also found by Cain ('47) that only lecithin and acid would stain blue appreciably with 1 per cent Nile Blue.

Further diagnostic tests were employed for the further verification and ic fication of the phospholipid group. The reaction of the phospholipids wit riodic acid in the PAS method and with the performic acid in the PFAS (P '51, Lillie '52) method was applied to appropriate sections. Both these oxid methods demonstrated a strong positive reaction in the distal cytoplasm c acinar cells. With the PFAS technique, the positive reaction may be reg as an indication of lipids, either phospholipids or cerebrosides, with unsatu bonds (Lillie '52). To further check on the ethylene groupings control sec treated with bromine (1 ml. bromine in 29 ml. C Cl_4) for one hour gave a tive PFAS reaction showing that the ethylene grouping was blocked. O other hand, the PAS reaction, after acetylation, gave a negative reaction suggests that the 1:2 glycol group was responsible for the original rea

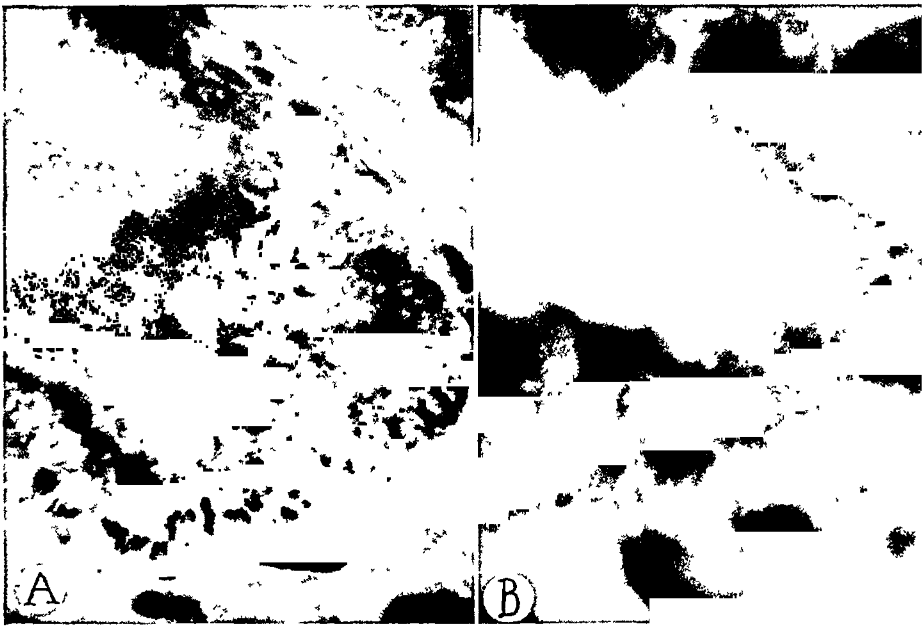

FIG. 5. *A*, an active secretory acinus may be lined with tall, simple columnar epit cells. Distal cytoplasm is filled with numerous discrete secretory granules. Note floc nature of secretion in acinar lumen. Fixation: Zenker-formol. Masson's trichrome ×1400. *B*, numerous small bodies are mitochondria. Fixation: Regaud's formalin bichr anilin acid fuchsin methyl green method of Bensley. ×1388.

(Gersh '49) It is apparent then that both ethylene and glycol grouping are present in the distal acinar cytoplasm

Further confirmatory evidence on the presence of the ester phosphatides in the acinar epithelium was supplied by the use of the tartaric-thionin mixture of Feyrter ('36), which revealed a definite metachromasia in the distal cytoplasm of the acinar cells There is no doubt, according to Pearse ('51), that the phosphatides are the principal lipid substances demonstrated by Feyrter's method and this is presumably on account of the phosphoryl group which induces the metachromasia Using the same method, Feyrter ('36, '42), and Pictl ('48) describe the metachromatic reaction of the lipoids and lipoprotein in the prostate of men However, interference due to the presence of mucopolysaccharides and their characteristic metachromasia already demonstrated in the prostate (by Arcadi '52) make it difficult to ascertain small quantities of combined lipids such as lecithoprotein or other proteinphosphatide complexes In addition, the metachromasia may have been enhanced by the acidic nature of the phospholipids as revealed by the use of Cain's ('47) method employing Nile Blue sulfate

This entire lipid picture is further complicated by the fact that the acetal phosphatides are found in constant association with the ester phosphatides (Pearse '53) As a specific diagnostic procedure for the acetal phosphatides, Arcadi ('52), using the plasmal reaction of Hack ('52), observed that the reaction was strongly positive throughout the cytoplasm of the acinar cells Pictl ('48) reported that after using both the Feulgen type of plasmal reaction and the Feyrter ('36) metachromatic reaction, the glandular epithelium of the prostate definitely showed the presence of a lipid-protein

BIREFRINGENT LIPOIDS

Examination of unstained sections and with polarized light revealed birefringent lipids The distribution of the birefringent material both in the epithelium and the connective tissue was not constant (Kinoshita '20, Kunze '22) even within the same prostate Anisotropic material could be found either 1) in the form of fine particles rather evenly distributed through the epithelium and including connective tissue, or 2) the birefringent particles could be heavily concentrated only in some localized areas of both the epithelium and underlying connective tissue (fig 3, *B*) Occasionally, birefringent material was seen in the acinar lumen In our study, the birefringent lipids correlated with the localization and identification of the neutral fat This fact was also observed earlier by Kinoshita ('20) These concentrations of lipid material could not be correlated with any observable pathological or secretory change No Maltese cross birefringency as is usually associated with cholesterol and its esters was observed

The birefringence of lipids, as has been pointed out by both Lison ('36) and later by Pearse ('53), is due to the physical state of the fat which directly influences its birefringency The failure to form spherocrystals and the resulting Maltese cross type of birefringence cannot be taken as an indication of the absence of cholesterol esters and lipids Kinoshita ('20) reports the Maltese cross type of birefringency in both the prostatic epithelium and secretion in man

The presence of cholesterol and its esters was revealed by a strong positive, but diffuse blue-green reaction in the prostatic epithelium when the Lieberman-Burchardt reaction, and the Schultz method (Romieu '27 modification) were used. Further confirmatory evidence on the presence of cholesterol was obtained by using a .5 per cent alcoholic solution of digitonin. The digitonin-cholesterol complex both in the acinar epithelium and the connective tissue became evident. Subsequent staining of the digitonin-treated sections with Sudan III revealed that the cholesterol esters in the epithelium became colored and lost their birefringence, while the crystals of the cholesterol-digitonin complex in the underlying connective tissue remained anisotropic and colorless. No free cholesterol was found by Kunze ('22) in the epithelial cells of the secretory acini. No cholesterol was detected in the lumen of the acini, although Kinoshita ('20) reports this to be of frequent normal occurrence in man.

SUMMARY

Histochemical investigations show that lipids form a major component of the prostatic epithelium and secretion in the dog.

The lipids of the acinar epithelium are predominantly neutral fat; the remainder consists of phospholipids, cholesterol, and cholesterol esters. There is evidence to indicate that in all probability most of the phosphatide is lecithin, but no lecithin could be demonstrated in the acinar lumen.

Birefringent lipids, possibly neutral fat, cholesterol and its esters are localized in both the epithelium and stroma. Cholesterol is absent in the acinar lumen.

The author wishes to express her thanks to Mr. J. Jackson, Emory University, Georgia for his aid in preparing the photographs.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

SCLEROSING LIPOGRANULOMAS OF THE MALE GENITALIA: REPORT OF ONE CASE AND REVIEW OF THE LITERATURE

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Tumors of the scrotum and shaft of the penis are rare. Localized sclerosing lipogranulomas of the male genitalia are extremely infrequent and information regarding their clinical behavior and histogenesis is not encountered in most standard textbooks of pathology, urology and urological pathology. The first published reference which we were able to find was in the Atlas of Genito-Urinary Pathology of the Armed Forces Institute of Pathology where Friedman and Ash state: "The lipoid granuloma of the testicular adnexae is a troublesome lesion, because it may simulate a tumor clinically and tuberculoid granuloma histologically." Hinman and Johnson in 1939 described 3 cases of acute traumatic fat necrosis of the scrotum in children followed by tumor-like lesions, but these resolved in a few weeks without therapy. Brown and Joergenson reported a case of "scrotal paraffinoma" in 1947, following injections of paraffin oil to the scrotum. Not a single instance of lipogranuloma was mentioned by Hinman and Gibson in an extensive review of tumors of the epididymis, spermatic cord and testicular tunics.

The first authenticated report of sclerosing lipogranuloma was that of Powell and Powell in 1948. The growth was originally diagnosed as a benign adenomatoid tumor of the testicular tunics but in consultation with the Armed Forces Institute of Pathology it was felt that "the process is akin with what has been called here sclerosing lipogranuloma. There are a few identical cases in the files and their nature is a mystery. In one patient the subcutaneous tissue of the entire scrotum and penis became progressively involved."

In 1950 Smetana and Bernhard analyzed all the cases seen at the Armed Forces Institute of Pathology of this peculiar, localized, reactive process which sometimes followed injury to the subcutaneous tissues and for which the term "sclerosing lipogranuloma" was coined. They reported 14 cases, nine of which occurred in the male genitalia, including the one previously reported by Powell and Powell. Although intimately related to other well known lipogranulomas of miscellaneous origin like fat necrosis of the female breast, relapsing nonsuppurative panniculitis of Weber Christian, lipid pneumonia, adiponecrosis subcutanea neonatorum, pelvic lipogranulomas caused by injections of iodized oils during uterosalpingography and other experimental lipogranulomas; it presented certain clinical and even pathological characteristics of its own to warrant its separation as an individual clinicopathological entity. Two additional cases appeared in the literature during 1952.

After a careful perusal of the literature one is impressed with the great difficulty of correct clinical appraisal of the lesion and the variety of clinical diag-

Accepted for publication September 21, 1955.

TABLE 1 *Analysis of all reported cases of sclerosing lipogranuloma of the male genitalia*

Case	Age	Race	Location	Size of Lesion	Previous Trauma	Symptoms	Clinical Diagnosis	Histopathologic Diagnosis
1 Smetana et al *	37	W	Scrotum and around testes	14 × 13 × 11 cm	None	None		Adenomatoid tumor
2 Smetana et al	34	W	Shaft of the penis	10 × 4 × 4 cm	Blow to penis 5 wks before	Swelling and discoloration	Acute fat necrosis	Fat necrosis
3 Smetana et al	20	W	Shaft of the penis	5 cm	None	Swelling, redness and tenderness	Reaction to poison ivy	Lymphangiomatosis of penis due to dermatitis
4 Smetana et al	25	W	Both tunica vaginalis testes	4 × 2 cm and 4 × 3.5 cm	None	None		Lipoma of tunica vaginalis with fat necrosis
5 Smetana et al	36	N	Tunica vaginalis testes	5 × 4 × 2.5 cm	None	None		Granuloma consistent with adenomatoid tumor
6 Smetana et al	23	N	Scrotal septum	4 × 2 × 1.5 cm	None	None		
7 Smetana et al	47	W	Cul de sac, seminal vesicles and prostate	Two pieces—5 × 2.7 × 1.5 cm and 3 × 1.6 × 1 cm	None	Difficulty in starting urination		
8 Smetana et al	35	W	Scrotal raphe and symphysis pubis	6 × 4 cm and 5 × 3.5 × 3 cm	Blow to scrotum one year ago	Swelling, discoloration and tenderness		Lipogranulomatous process
9 Smetana et al	60	W	Epididymis		Blow to testicle 10 yrs before	Swelling of scrotum, slight pain		
10 Manning	64	W	Shaft of penis	12 × 6 cm	None	Tight prepuce with difficulty in voiding		Sclerosing lipogranuloma
11 Galbraith and Young	52	W	Scrotum extending to anterior abd wall	15 × 9 × 8 cm (scrotal mass)	Aspiration of hydrocele	Swelling and redness with tenderness		Weber Christian disease, sclerosing lipogranuloma
12 Marcial	39	N	Scrotal raphe	5 × 3 × 1 cm	None	None		

nosis such as fibrous mass of the penis, swelling of the penis, tumors of both testes, tumors of the scrotum, seminoma of the testicle. The difficulty in histopathologic diagnosis is also evident among pathologists and diagnoses of granulomatous inflammatory tissue, fat necrosis, adenomatoid tumor, and even adenocarcinoma have been offered.

The lack of familiarity with this lesion among most clinicians and general pathologists, the obvious difficulty in establishing its correct clinical and pathologic diagnosis and the infrequency of the lesion prompted us to report our case and review the literature.

CASE REPORT

A 39-year-old Negro was seen for the first time at the Isaac González Martínez Oncologic Hospital complaining of a painless mass between both testicles of 3 years' duration. There was no history of trauma, swelling or inflammatory reac-

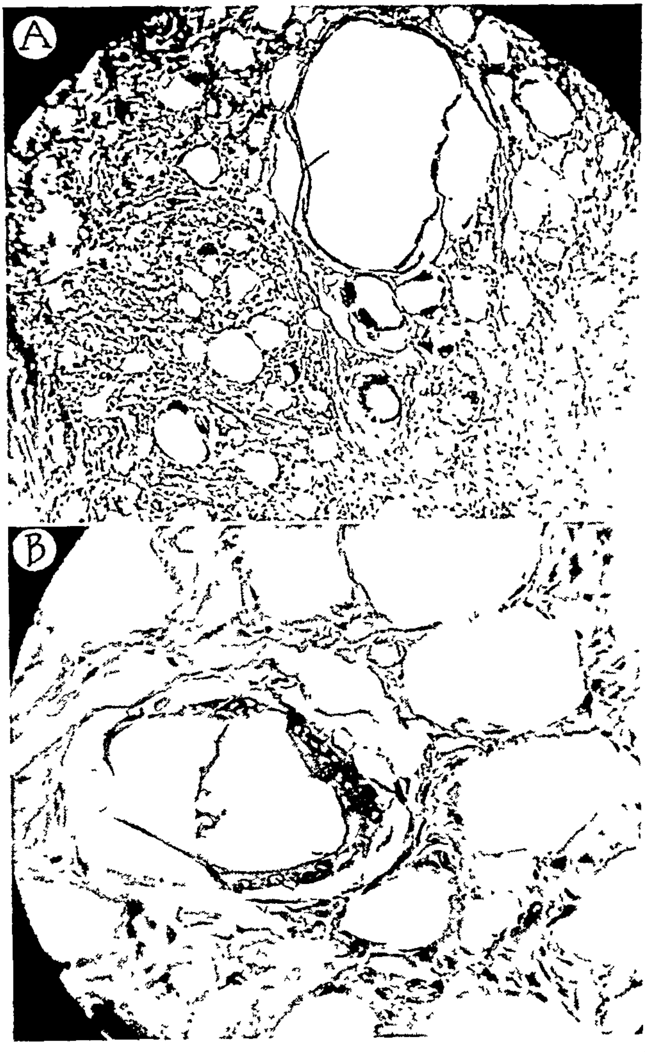

FIG. 1. *A*, numerous large globules of fat forming cyst-like spaces lined with endothelium or flattened giant cells of foreign body type. *B*, higher magnification of cyst-like spaces which are sometimes confused with mesothelial ones of adenomatoid tumors.

tion of the skin of the scrotum. The mass had only slightly increased in size since first noted. It was elongated, freely movable, located at the scrotal raphe and completely independent from both testes. There were no other pertinent findings in the physical examination. The preoperative diagnosis was that of "indurated tumor of the scrotal sac, clinically benign, etiology to be determined." The lesion was widely excised.

The mass was ovoid and measured 5 by 3 by 1.5 cm. It was firm, rubbery and on section composed of yellowish-orange tissue traversed with numerous grayish-white fibrous septa and exhibiting several minute cystic spaces not over 1 mm. each. Microscopically the normal structure of the subcutaneous fat was completely disrupted. The stromal septa had undergone hyaline necrosis which had permitted fat droplets to coalesce into large globules of various sizes separated by fibrous connective tissue. Many cyst-like spaces lined with endo-

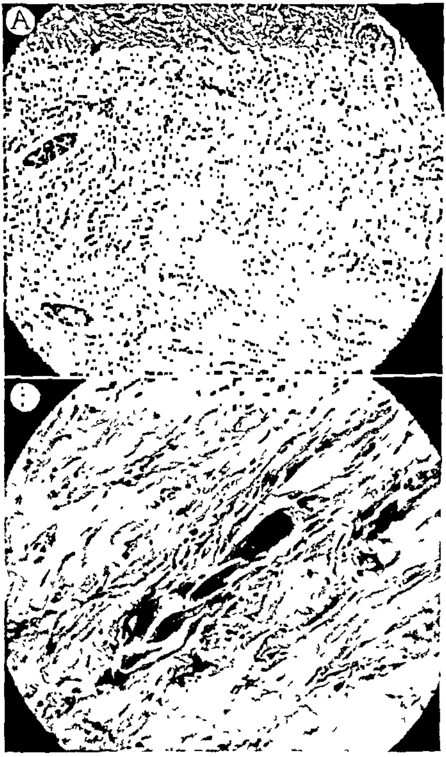

Fig. 2. *A*, prominent sclerosis and replacement of fat by collagen fibrous tissue. *B*, foreign body giant cells caught between actively proliferating fibrous tissue.

thelium or more frequently by syncytial giant cells of the foreign body type were encountered throughout the tissue. Many of these cyst-like spaces were surrounded by dense and deeply eosinophilic collagen tissue, in places distorting the spherical appearance of the globules. Numerous macrophages containing phagocytosed fat and moderately heavy round cell infiltration were seen around many of the blood vessels. In places there was dense scarring and hyalinization of the stroma. Plasma cells were infrequent and polys and eosinophiles were not seen. Sudan 3 demonstrated sudanophilic material within the cystic spaces and in the vacuoles of the distended macrophages.

Comment: The pathogenesis of sclerosing lipogranuloma is not entirely clear. Apart from the history of trauma in four of the cases already reported in the literature, there seems to be no known cause for the condition. There is necrosis of fat cells with subsequent liberation of fat globules. The latter act as a foreign substance provoking a granulomatous reaction as previously described. There is no available explanation at present for the persistence and less for the extension and progression of the process. In none of the cases reported has there been spontaneous regression of the lesion, and the best curative procedure, when possible, has been surgical excision. In some instances the process has recurred and progressed relentlessly to extend into adjacent tissues acting as a neoplasm.

The lesion occurred in men between the ages of 20 and 64; two-thirds of the cases in men below the age of forty. Nine of the patients were white persons and three were Negroes. The duration of onset to operation varied from 5 weeks to 10 years. In five of the patients there were no symptoms referable to the "tumor."

SUMMARY

The twelfth recorded case of sclerosing lipogranuloma of the male genitalia is presented and a review of the literature attempted.

The numerous problems encountered in the diagnosis and clinical management of the lesion are mentioned.

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The Journal of Urology
Vol 75 No 2, February 1956
Printed in U S A

CLINICAL RESPONSE OF URINARY TRACT INFECTIONS TREATED BY ELKOSIN, GANTRISIN, TRIPLE SULFA OR TRIPLE SULFA-ACHROMYCIN

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There is much in the literature of the effectiveness of the various sulfonamides in the treatment of urinary tract infections Schweinberg and Rutenburg[1] found elkosin superior to gantrisin, while Lehr[2] felt that his results indicated gantrisin to be superior to triple sulfa mixtures Rhoads et al [3] believed gantrisin to be the drug of choice for most urinary tract infections The usefulness of combinations of sulfonamides and antibiotics has been reported by Rhoads et al,[3] Leadbetter and Woodruff[4] and Eisenberg et al [5] A recent paper indicated the new antibiotic, tetracycline, to be effective in treating urinary tract infections [6]

This paper reports a clinical and bacteriological evaluation of the use of elkosin, gantrisin, triple sulfa, and triple sulfa-achromycin* on a total of 80 patients The results suggest that the three sulfas are about equal while the combination is more effective particularly against resistant organisms

METHODS

Adults from 21 to 75 years of age, mainly women, were treated without selection using one of the four agents Most were uncomplicated cases of cicatricial urethritis or urethrotrigonitis Dosage consisted of 4 gm daily of elkosin, gantrisin or triple sulfa, in divided doses, or ½ gm of triple sulfa and 125 mg tetracycline, 4 times daily Culture and routine urinalysis of a catheterized specimen from females and mid stream specimen from males was obtained before beginning treatment, 3–5 days and 10–12 days after initiation of treatment, and 2

Accepted for publication July 20, 1955
This investigation was supported by the Lederle Laboratories Division, American Cyanamide Company

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* *Elkosin*, trade name of 6 sulfanilamide 2,4 dimethyl pyrimidine manufactured by Ciba Pharmaceutical Products Inc *Gantrisin*, trade name of 3,4 dimethyl 5 sulfanilamide isoxazole manufactured by Hoffman LaRoche *Triple Sulfa*, trade name of sulfadiazine, sulfamerazine and sulfamethazine manufactured by Lederle Laboratories Division of the American Cyanamide Co *Triple Sulfa Achromycin*, trade name of a combination of the triple sulfa and tetracycline manufactured by the Lederle Laboratories Division of the American Cyanamide Company

TABLE 1. *Relation of species to treatment failures*

Organism	No. of Times Isolated	% Showing Treatment Failure
E. coli	45	18*
S. faecalis	12	83
A. aerogenes	7	59
Proteus	4	50
Other strep	5	0
Paracolon	3	0
Pseudomonas	3	33

* 2 of the 8 were mixed infections with S. faecalis.

TABLE 2. *Results of treatment*

Drug	No. Treated	No. Adequately Followed	% Failures	% E. coli	% A. aer.	% S. fec.	% Prot.
Elkosin	12	10	20	60	0	20	10
Gantrisin	21	17	35	70	12	6	0
TS	22	19	37	53	10	20	5
TS-Ac	25	25	12	68	12	12	8

weeks or more after cessation of treatment, whenever possible. A cure was considered established if cultures were negative 2 weeks or more after completion of treatment and the patient was symptom-free. Bacteriologic cultures and sensitivity tests on pure cultures of the isolated organisms were performed as reported in a previous paper.[7]

RESULTS AND DISCUSSION

Relative frequency of organisms associated with clinical failure. Table 1 shows the relative frequency with which various bacteria were isolated and the per cent of clinical treatment failures associated with each. Staphylococci were isolated in a few cases but were considered to be contaminants since all came from males and cultures of the urine of 15 "normal" males revealed staphylococci in twelve. Lazarus and Wood[8] also feel that these organisms are contaminants. Perhaps in the presence of clinical symptoms and the absence of any other bacteria they may be significant. The greatest percentage of failures was seen with Streptococcus faecalis, Aerobacter aerogenes, and Proteus species. These organisms and Pseudomonas species were usually resistant by the disk test.

Clinical results. Table 2 shows gantrisin and triple sulfa to have about the same percentage of failures. Elkosin has a somewhat lower percentage, but the number of cases is so small that the difference may not be significant. Triple sulfa-achromycin had the lowest percentage of failures, although the patients treated were infected with just as many of the refractory organisms as were those treated with the sulfas alone One patient treated with triple sulfa-achromycin had a mixed infection with S faecalis, Proteus and E coli which had failed to respond to triple sulfa She was cured with triple sulfa-achromycin A aerogenes was isolated from another and two 10 day courses of triple sulfa failed to eradicate it Cure was effected with triple sulfa-achromycin Three failures were noted with triple sulfa-achromycin One was a mixed infection with E coli, a Streptococcus, and a Staphylococcus The others were an infection due to a E coli previously treated with gantrisin and a mixed infection with Proteus and S faecalis in which latter case the drug was withdrawn because of a reaction before completing the treatment A mixed infection with Proteus, S faecalis and staphylococci and one with S faecalis failed to respond to elkosin Failures with gantrisin were due to two strains of A aerogenes, and two of E coli infection Those with triple sulfa were mixed infections of S faecalis, staphylococci and E coli, S faecalis and E coli, S faecalis and staphylococci, and two with A aerogenes and one each with Pseudomonas and Proteus The drug was withheld in the treatment of the Proteus infection because of a generalized drug reaction

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Seventy-five per cent of the failures were due to A aerogenes or S faecalis alone or in combination with another organism Four of the A aerogenes were resistant to sulfonamides, while all of the S faecalis were resistant Cure was apparently brought about by the triple sulfa achromycin combination because of the sensitivity of the S faecalis to the achromycin

No A aerogenes infections of the four treated with sulfonamides alone responded to treatment However, four of the strains were resistant Three A aerogenes infections did respond to treatment with triple sulfa-achromycin, but only one of these strains was resistant Two infections due to Proteus were not cleared by sulfonamides, while two others treated with triple sulfa achromycin did respond The latter two were mixed infections

This study again emphasizes the difficulty of treating infections due to A aerogenes and to mixed infections The combination appears to be more effective against each and in lower concentration than usually prescribed for both agents Some refractory cases were examined for blood and urine levels of both sulfonamide and achromycin, but they were as high as in other subjects in which the infection was controlled

SUMMARY

A total of 80 patients with urinary tract infections were treated with elkosin, gantrisin, triple sulfa and triple sulfa achromycin Triple sulfa-achromycin was much more effective than the single sulfonamides showing a failure rate of only 12 per cent in the treated 25 patients

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

ACUTE URINARY RETENTION DUE TO DRUGS

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Of the various drugs known to influence micturition in man some are capable of producing urinary retention by interfering with the bladder emptying mechanism. A number of these are in wide clinical use today. For the most part these medications affect bladder muscle function either by altering bladder muscle action or by causing profuse diuresis and consequent overdistention of the bladder. In both instances predisposing factors are important, and in our experience, the most significant of these are debility, recumbency and prostatism. The problem of acute urinary retention following the use of drugs occurs chiefly in middle aged and elderly men, but we have observed it at times in young, vigorous men as well as women.

The practicing physician needs to be familiar with the potential bladder effect of medications which he administers or prescribes, and must assess the bladder status of his patient prior to administration of any one of the drugs known to be capable of interfering with the bladder emptying mechanism.

In a previous article dealing with the problem of acute urinary retention following the use of parenteral mercurial diuretics for congestive heart failure, we emphasized the importance of assessing bladder status, particularly in middle aged and elderly men, before such treatment was instituted.[1] Not a few men of this age distribution have bladder symptoms, the result of varying degrees of obstruction of the bladder outlet, occasioned by prostatic enlargement. Most of these men accept the symptoms of slowed stream, slight diurnal frequency and nocturia as inevitable concomitants of the aging process. Without specific interrogation patients often fail to mention these symptoms, in the belief that they are normal or unimportant.

If a patient with already compromised bladder function is given a parenteral mercurial diuretic or one of the drugs to be discussed presently there is not only risk of acute urinary retention, but the distinct hazard that mere discontinuance of the medication will not suffice to restore bladder function to its previous state. Emergency surgery then may become necessary. On the other hand, when acute urinary retention from drug administration occurs in a patient with previously normal bladder function it is our experience that cessation of therapy is soon followed by re-establishment of the normal bladder state.

Since the relation of parenterally administered mercurial diuretics to acute urinary retention has been considered in a previous article,[1] our further concern in this presentation will be limited to other drugs.

REPORT OF CASES

Case 1. J. C., a white man aged 63, was admitted to the hospital for acute coronary thrombosis and posterior myocardial infarction associated with com-

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Accepted for publication September 21, 1955.

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plete A–V block and very frequent convulsive seizures (Stokes-Adams syndrome) The ventricular rate was 42 per minute Ephedrine sulfate, gr 3/8 was administered orally every 3 hours Convulsive episodes became less frequent during the succeeding 2 days, after which there were no further seizures There was no history of diurnal frequency, nocturia or dysuria On the third hospital day the patient complained of marked burning and frequency of urination, and then became unable to void Ephedrine was discontinued, and the bladder catheterized Digital rectal examination revealed minimal prostatic enlargement Several further catheterizations were necessary, after which the patient was able to void normally

Case 2 M B , a white man aged 61, had bronchial asthma over a period of 20 years Aside from nocturia (once) there had never been any symptoms referable to the urinary tract On the day preceding hospital admission an allergist administered 0 2 cc of epinephrine subcutaneously for a severe, asthmatic paroxysm The patient thereafter was not able to void, and catheterization was performed at home on three separate occasions On admission to the hospital examination disclosed a moderately enlarged, smooth prostate gland Continuous catheter drainage was unsuccessful because the patient could not tolerate an indwelling catheter On the day following admission suprapubic cystostomy was performed under local anesthesia with the patient in the sitting position because of the continuing asthmatic state Ten days later a second stage prostatectomy was done At discharge from the hospital the bladder status was normal

Case 3 A J , a white man aged 61, was known to have had symptoms referable to duodenal ulcer for 6 years One month prior to admission to the hospital a gastroenterologist prescribed methantheline (banthine) bromide, 50 mg every 6 hours, for intractable hiccup associated with hematemesis While the patient had never sought medical advice for bladder symptoms, he had slight diurnal frequency and nocturia (two to three times) Within several days, the patient complained of increasing diurnal frequency, nocturia (four times) and dribbling, but the medication was continued, evidently because the attending physician felt it to be efficacious in controlling the ulcer symptoms and hiccup One month after the onset of bladder symptoms examination disclosed a decidedly distended bladder and a moderately enlarged, uniform, semifirm prostate gland Methantheline (banthine) bromide was discontinued, and continuous catheter drainage instituted for a period of 4 days Removal of the catheter was followed by a return of bladder symptoms associated with a large volume of residual urine A two stage prostatectomy was performed with uneventful recovery and return of bladder status to normal

Case 4 G H , a white man aged 58, had a subtotal gastrectomy for duodenal ulcer 3 years before admission to the hospital Four days before admission a physician prescribed oxyphenonium (antrenyl) bromide for symptoms believed to be due to recurrent ulcer The patient, who had previously disregarded slight diurnal frequency and nocturia (twice), soon noted increasing frequency and difficulty of micturition On the day preceding admission acute urinary retention ensued Immediately after admission examination disclosed a decidedly distended bladder and moderately enlarged, smooth prostate gland Continuous bladder drainage with a Foley catheter was instituted, and bethanechol (urecholine) chloride administered subcutaneously, 5 mg. every 4 hours. Three days later the catheter was removed and urecholine discontinued. Acute urinary retention again ensued. A two-stage prostatectomy was performed, with subsequent return of bladder status to normal.

Case 5. A. B., a white man aged 30, was hospitalized for acute coronary thrombosis and anterior myocardial infarction. He received large amounts of meperidine (demerol) hydrochloride for relief of severe anterior chest pain over a period of several days. There had never been any symptoms referable to the urinary tract. On the third hospital day the patient complained of increasing frequency of urination, tenesmus and difficulty in micturition. Acute urinary retention ensued, requiring bladder catheterization. The patient remained unable to void, and twelve hours later continuous catheter drainage was instituted. The catheter was removed when the patient became ambulatory, three weeks after admission. The bladder status then quickly reverted to normal.

COMMENT

The physiology of micturition is not very clear. Its components are complex.[2, 3] Normal detrusor action by cholinergic stimulation results in reciprocal bladder wall contraction and vesical neck relaxation.[2] Anticholinergic effect on the bladder is associated with relaxation of the bladder wall and vesical neck constriction. The explanation for this reciprocal action between the detrusor muscle and vesical bladder neck is unknown.[3]

The most interesting development in the field of anticholinergic drugs in recent years has been the synthesis of new quarternary ammonium compounds which, in therapeutic doses, block parasympathetic ganglia and effector sites. In much larger doses they also block sympathetic ganglia and neuromuscular end plates. Methantheline (banthine) bromide was the first of these in clinical use. Its effect in the treatment of gastrointestinal disorders, chiefly peptic ulcer, depends upon its action in decreasing secretions and motility. It has also been advocated in ureteral and vesical spasm, hyperhidrosis and for the control of salivation.[4, 5]

Case 3 is an example of acute urinary retention which we believe was the result of administration of this drug.[6, 7] Anticholinergic effect on bladder muscle function and consequent relaxation of bladder wall and vesical neck constriction resulted in acute urinary retention in a patient with already compromised bladder function due to prostatic enlargement. Case 4 is an instance of similar difficulty attributed to the use of oxphenonium (antrenyl) bromide Other drugs of similar pharmacologic action, and therefore with potentially the same effect on the bladder mechanism, are propantheline (pro banthine) bromide, diphemanil (prantal) methylsulfate, methylscopolamine (pamine) methylsulfate and tricyclamol (tricoloid) Recently a new anticholinergic drug has been advocated as being effective in peptic ulcer without the threat of urinary retention*

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Case 1 is an example of acute urinary retention believed to be due to administration of ephedrine[8, 9] Fortunately, the patient's bladder status became normal after the discontinuance of the drug, and his course continued uneventfully without this or similar medications Epinephrine is rarely the cause of bladder symptoms, probably because the duration of its effect is short,[8] differing in this respect from ephedrine, whose pharmacologic action is much more prolonged Nevertheless, in case 2 we believe that acute urinary retention was precipitated by the use of epinephrine

Ephedrine and congeners intensify the normal adrenergic innervation of the bladder, believed to oppose cholinergic innervation, and therefore have an effect on bladder function similar to that of anticholinergic drugs Other drugs in this category are amphetamine (benzedrine) sulfate, phenylephrine (neosynephrine) hydrochloride, naphazoline (privine) hydrochloride, mephentermine (wyamine) sulfate, methamphetamine (methedrine) hydrochloride, etc

Ganglion blocking drugs have recently come into medical use for the treatment of hypertension Perhaps the best known among these are hexamethonium and pentolinium tartrate (ansolysen) Both block sympathetic and parasympathetic ganglia Among the many side effects of hexamethonium acute urinary retention has been reported[10, 12] Freis has stated that none of his patients under treatment with pentolinium tartrate suffered from inability to empty the urinary bladder[11]

Apresoline, likewise widely used in the therapy of hypertension, has been reported to be responsible for difficulty in voiding with hypotonia of the bladder The mechanism of this phenomenon is not clear[13]

Antihistaminic drugs have also been incriminated in the causation of acute urinary retention Wolfson reported an instance following ingestion of tripelennamine (pyribenzamine) hydrochloride[14] Uhle and Knoch mentioned several cases of difficult urination and one case of acute urinary retention following administration of phenindamine (thephorin) tartrate.[2] We have likewise observed bladder symptoms in a 56-year-old man given diphenhydramine (benadryl) hydrochloride for allergic rhinitis. Symptoms indicative of impending acute urinary retention cleared up after discontinuance of the drug, with reversion of bladder status to normal.

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* Piptal, H L Darell, M D scientific director of Lakeside Laboratories, Inc, Milwaukee, Wis personal communication

[8] Balyeat, R M and Rinkel H J Urinary retention due to use of ephedrine J A M A 98: 1545–1546, 1932

[9] Boston, L N Dysuria following six cases of ephedrine therapy M Times, New York, 56: 94 1928

[10] Grimson K S and others Caution with regard to use of hexamethonium and apresoline J A M A, 149 215–220, 1952

[11] Freis, E D and others A clinical appraisal of pentapyrrolidinium (M & B 2050) in [illegible] 540 546, 1954

[illegible] antihypertensive drugs Am J Med, 17 70-83 1954

[illegible] and Cohen, S H Bladder disturbances due to [illegible] -526, 1952

[14] Wolfson S A Urinary obstruction due to tripelennamine hydrochloride J A M A, 140 958 1949

The antihistamines, among other pharmacologic effects, are known to have anticholinergic and adrenergic actions.[15] The mechanism by which these agents produce bladder symptoms is believed to be an anticholinergic effect of detrusor weakness and sphincter spasticity.[2]

Van Duzen has also listed the following antihistaminic drugs as provocative of bladder symptoms[16]: chlorprophenpyridamine (chlor-trimeton) maleate, methapyrilene (histadyl) hydrochloride, thonzylamine (anahist) hydrochloride and chlorcyclizine (perazil).

There is little doubt that morphine and other narcotic drugs are important contributing factors in the production of acute urinary retention, especially in debility, recumbency and prostatism. Van Duzen et al. believe that morphine causes stimulation of the bladder detrusor and the muscle of the vesical orifice; the latter muscle is stronger than that of the fundus, and so retention may result.[17]

Sulfadiazine ingestion has produced acute urinary retention by deposition of crystals in the urethra at the external meatus.[18]

In our opinion, no patient with symptoms of prostatism should receive anticholinergic, adrenergic, ganglion blocking, antihistaminic drugs or opiates unless the need is compelling. Under these circumstances the smallest doses feasible should be prescribed, and the medication discontinued at the earliest possible moment. During administration of such drugs great vigilance should be exercised with regard to bladder status. Symptoms of increased urinary frequency, nocturia, slowing of urinary stream and other bladder symptoms may not be volunteered by the patient. The physician often can disclose their presence only by specific inquiry. More definitive information in regard to bladder status can be obtained by determining the volume of residual urine. To disregard such symptoms and continue with the use of a drug in any of the above categories may result in acute urinary retention.

As soon as bladder symptoms appear the offending drug should be discontinued. Usually, in the absence of prostatism, this will suffice for the return of bladder function to normal, but occasionally catheterization will be necessary. When acute urinary retention is precipitated by a drug in a man with antecedent prostatic symptoms conservative measures may not suffice. Often surgery becomes necessary.

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[15] Loew, E. R.: Pharmacology of antihistaminic compounds. Physiol. Rev., **27**: 542–573, 1947.

[16] Van Duzen, R. E.: Pharmacological effect of various drugs on micturition. J. A. M. A., **156**: 1393–1396, 1954.

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[18] Biorn, C. L.: Anuria owing to urethral obstruction by sulfadiazine crystals. Calif. Med., **77**: 196–197, 1952.

SUMMARY

Various drugs having an effect on the bl emptying mechanism are discussed

Cases are reported in which acute urinary ention followed the administration of drugs

The mechanism of action on bladder fun of anticholinergic, adrenergic, ganglion blocking and antihistaminic drugs esented

Precautionary measures and treatment ar iefly considered

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

PARAPLEGIA, A RARE COMPLICATION OF TRANSLUMBAR AORTOGRAPHY

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In recent years interest in translumbar aortography has increased considerably. The important diagnostic value and relative safety of this procedure are universally accepted and practiced. Because of its wide use one should expect to encounter some complications. In an editorial on arteriography published in the *Journal* of the American Medical Association, January 1952,[1] the statement is made that the consensus of opinion is that translumbar aortography is safer and simpler than the method of retrograde catheterization of the femoral artery. However, one must realize that translumbar aortography is not without potential danger.

Melick and his coworkers[2] reviewed the present status of aortography and stressed three possible dangers attending this procedure, viz., 1) hemorrhage from the puncture site in the aorta, 2) necrosis of the intestines resulting from inadvertent injection of the contrast directly into the superior mesenteric artery, and 3) sensitivity reactions to the contrast medium. Wagner and Price[3] and Melick, Yarbrough and Boler[4] reported fatalities due to necrosis of the intestines following the injection of 80 per cent sodium iodide into the superior mesenteric artery at time of aortography.

Gould and Willson (1954)[5] made an extensive review of the various complications of translumbar aortography and found the most common complication to be serious renal damage, which occurred in 14 cases. In 6 cases the contrast medium was injected directly into one renal artery with resultant severe renal damage and no fatalities. In 8 cases, the contrast medium was injected into the aorta and bilateral renal shutdown occurred, which was fatal in 2 cases. The majority of the 8 patients had a high aortic obstruction and several had severe pre-existing renal damage. Josselson and Kaplan (1954)[6] subsequently reported a fatal case of anuria following translumbar aortography with neo-iopax.

The purpose of this paper is to report another case of the unusual complication of complete paraplegia following translumbar aortography. The literature contains very few reported cases, viz., 1) Antoni and Lindgren (1949),[7] 2) Boyarsky (1954),[8] and 3) Baurys (1954).[9] Baurys stated that Nelson[10] was

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Accepted for publication September 21, 1955.

[1] Editorial on aortography. J. A. M. A., **148:** 162, 1952.

[2] Melick, W. F., Byrne, J. E. and Boler, T. D.: J. Urol., **67:** 1019, 1952.

[3] Wagner, F. B. and Price, A. D.: Surgery, **27:** 621, 1950.

[4] Melick, W. F., Yarbrough, C. P. and Boler, T. D.: J. Urol., **66:** 458, 1951.

[5] Gould, D. M. and Willson, J. K.: Am. J. Med. Sci., **228:** 586, 1954.

[6] Josselson, A. J. and Kaplan, A. H.: J. Urol., **72:** 256, 1954.

[7] Antoni, N. and Lindgren, E.: Acta Chir. Scandinav., **98:** 230, 1949.

[8] Boyarsky, S.: J. A. M. A., **156:** 509, 1954.

[9] Baurys, W.: Urologist's Correspondence Club, Oct. 5, 1954; idem, Personal communication.

[10] Nelson: Quoted by Baurys, loc. cit.

acquainted with two additional cases occurring in Europe and Canada respectively. The details in these 2 cases are lacking, except that in both patients complete paraplegia developed and they survived.

In the reported cases the chief symptoms of this complication are paraplegia with loss of reflexes (areflexia), loss of response to light and painful stimuli (anesthesia and analgesia), loss of response to heat and cold (thermanesthesia), and loss of bladder control.

Antoni and Lindgren's patient was a 68-year-old man with arteriosclerosis and peripheral vascular occlusion. He died 3 months after the onset of gangrene of a leg that followed aortography with 70 per cent iodopyracet.

Boyarsky's patient was a 63-year-old man with evidence of peripheral and retinal arteriosclerosis who complained of low abdominal cramps due to an aneurysm of abdominal aorta. Paraplegia developed immediately after aortography with 70 per cent sodium acetrizoate (urokon sodium) The patient made a partial recovery from the paraplegia and 2 months later he was ambulatory with crutches, but had a partial spastic paresis of both lower extremities. He regained his control of urination and had no residual urine

Baurys's patient was a 68-year-old woman with a right renal cyst. Following translumbar aortography (type of contrast medium not mentioned), she experienced complete loss of motor power and pain perception, which persisted for 3 weeks without change when she died suddenly with a temperature of 103F of undetermined origin. Unfortunately, permission for autopsy was not granted.

CASE REPORT

H. E., a 52-year-old white man, married, painter, was referred by Dr. Joseph Skloven. He was admitted to the urological service of the Sinai Hospital on October 25, 1953 complaining of pain in both loins of 2 weeks' duration. The pain was described as dull, gnawing, intermittent, and annoying. One week prior to admission a plain film of the abdomen was taken by his family physician, and the patient was told that he had a calcified mass in the left kidney region and a stone in the right kidney. Hospitalization and further study were advised.

Past history disclosed treatment for lead poisoning in 1925 acquired as a result of his occupation as a painter. In 1926 he had an accident and sustained several fractured left ribs with left lung complications. He had no history of tuberculosis, syphilis, or allergic disease.

Physical examination was essentially negative except for the presence of a firm, globular, nontender mass in the left lumbar region, which did not move during respiration. Blood pressure was 120 mm. Hg systolic and 80 mm. Hg diastolic. The hematocrit, red blood count, white blood count and differential count, blood sugar, blood urea, serologic test for syphilis, urinalysis, and electrocardiogram were within normal limits.

On October 22, 1953, excretory urography revealed the right kidney to have a normal pattern, and the left kidney did not fill. There was a large calcified mass in the left retroperitoneal area, which was regarded as probably renal in

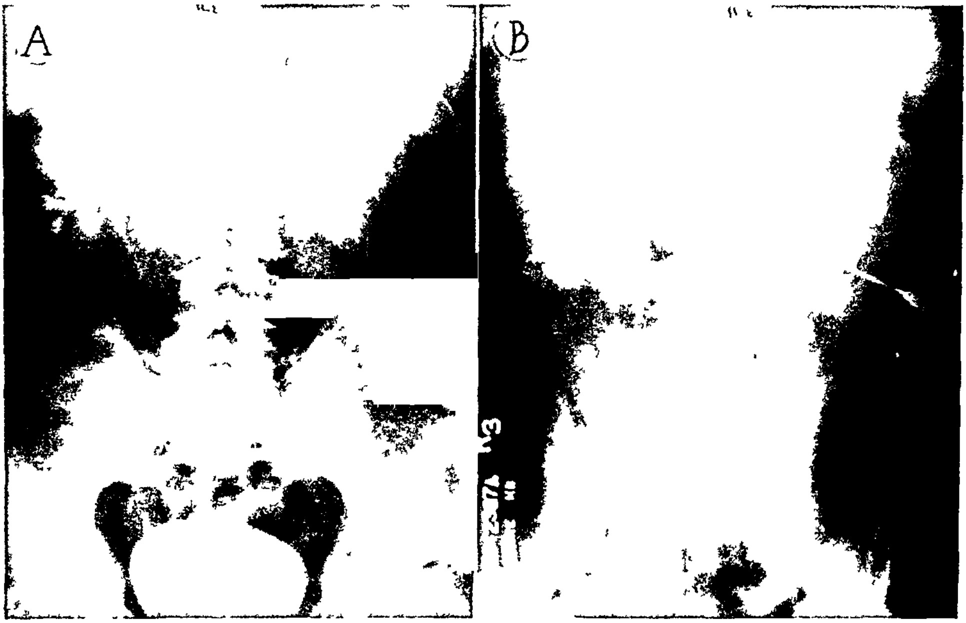

FIG. 1. *A*, excretory urogram (15-minute film) showing normal right kidney and large calcified shadow in left renal area. *B*, aortogram showing normal blood supply of right kidney and displaced renal artery supplying left renal mass. Calcified mass appears attached to kidney area.

origin (fig. 1, *A*). Barium enema and gastrointestinal series were not remarkable except for multiple small diverticula in the sigmoid. On October 29, 1953, cystoscopy and retrograde pyelography were performed. There was a slight prominence of the posterior portion of the vesical neck due to median bar formation. The right ureteral orifice was normal in size, shape, and position, and was easily catheterized with a 6F ureteral catheter. The left orifice appeared as a faint dimpling and could not be catheterized. On November 2, 1952 translumbar aortography under 2 per cent pentothal anesthesia was carried out with the patient in the prone position on the x-ray table. The usual No. 18 gauge long needle used for aortography was easily introduced into the aorta at the level of the second lumbar vertebra. A preliminary injection of 2 cc of 70 per cent urokon was made directly into the aorta as a sensitivity test with no reaction. During the injection of 30 cc of 70 per cent urokon, the patient had generalized convulsions, which were more marked in the lower extremities and trunk, and lasted about ten seconds.

The configuration of the right renal vessels was normal. A smaller vessel is seen partially filled and extending upward toward the region of the left kidney. This probably represented the left renal artery. There is no vascular pattern noted around or within the previously described cystic calcified mass. The remaining visualized aortic branches are grossly normal (fig. 1, *B*).

The patient was returned to the ward in fairly good condition. After he had fully recovered from the anesthesia about six hours later, he was unable to move his lower extremities. Examination at this time revealed complete flaccid paralysis of both lower extremities with loss of tendon reflexes at both knees and ankles.

The reaction to pain and temperature was absent below the level of the eighth thoracic vertebra The right foot could be slightly flexed and extended Sensation of vibration and position was good

The next morning Dr Clinton Harrison, attending neurosurgeon, examined the patient and confirmed the aforementioned findings His impression was thrombosis of the anterior spinal artery or spasm of this artery following injection of the contrast medium Mechanical compression of the spinal cord was ruled out as there was no dynamic block on lumbar puncture done on November 4, 1953 The spinal fluid was clear and under normal pressure, the spinal fluid sugar was 68 mg per cent and the total protein was 420 mg per cent No evidence of vertebral fracture was present on the roentgenograms of the spine The patient was unable to void and an indwelling urethral catheter (18F Foley with 5 cc bag) was inserted and connected up to a McKenna tidal irrigation apparatus in order to develop an automatic bladder He moved his bowels involuntarily in bed

He showed a gradual and progressive improvement for on November 11, 1953 the sensory levels of pain and temperature were equivocal at the level of the eighth thoracic vertebra and positive at the eleventh and twelfth thoracic vertebrae The response to touch and vibration continued good Despite good nursing care, a decubitus ulcer developed and the patient was placed on a Stryker frame On December 12, 1953, he could flex his right knee slightly and move the right foot freely in any direction The left toe could be moved to a lesser degree Pain and temperature responses remained unchanged Physiotherapy and massage were initiated in an effort to preserve and improve the muscles of his legs and back

On December 18, 1953, cystometric study revealed a mildly hypotonic bladder with fairly good bladder contractions and frequent uninhibited contractions Bladder sensation of fullness was absent The Foley catheter was removed and he voided at intervals of four to five hours aided by simultaneous manual compression of the bladder The residual urine was 40 cc

On March 8, 1954 the patient began to complain of pain in the chest and left hip, and the decubitus ulcer recurred He became anorexic and lost weight On April 18, roentgenographic study revealed metastases in the lungs, ribs, clavicle, pelvic bones, and lumbar vertebrae His course was progressively downhill, and he expired on April 27, 1954 of generalized carcinomatosis

A postmortem examination was performed about two hours after death The positive findings included 1) malignant Grawitz tumor of upper pole of left kidney, 2) metastases to adrenals, liver, periportal, periaortic, and inguinal lymph nodes, left clavicle, ribs, vertebrae, and skull, 3) encrusted cystitis, 4) calcification of hydronephrotic left kidney, 5) coronary heart disease, 6) arteriosclerosis, 7) pulmonary emphysema and atelectasis, 8) benign hypertrophy of the prostate The spinal cord was removed intact for further study Careful study did not reveal any thrombosis or occlusion of the anterior spinal arteries by tumor cells or organized blood clot

Histological examination of the spinal cord was made by Dr John Wagner, consultant in neuropathology, Department of Laboratories. "Sections from the lower cervical, thoracic and thoracolumbar spinal cord were stained with hematoxylin and eosin. The nerve roots and meninges are apparently normal and without evidence of inflammatory change. In the cervicothoracic area, scattered fresh petechial hemorrhages and moderate congestive changes were found. The ventral horn cells in the thoracic and thoracolumbar areas are slightly reduced in number and showed pigmentary changes, particularly in the thoracic areas. The dorsal horn cells were also slightly reduced in number.

"The most conspicuous lesion is an irregular sort of demyelination occupying principally the ventrolateral areas of the lateral funiculi and most of the ventral funiculus throughout all the section examined. A few irregular areas of demyelination are seen adjacent to the dorsal sulcus. The ventral areas of demyelination appear continuous with the ventral nerve roots, but in some sec-

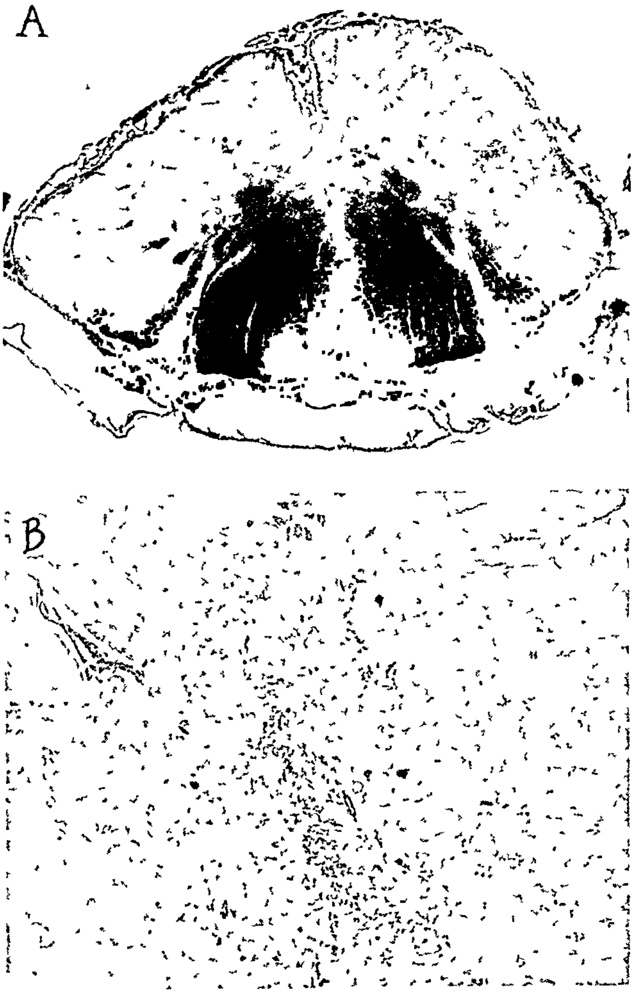

FIG. 2 Photomicrographs *A*, section of thoracic spinal cord showing areas of demyelination occupying principally ventrolateral areas of lateral funiculi and most of ventral funiculus *B*, section (low power) of thoracolumbar portion of spinal cord showing presence of macrophages and dissolution of tissue in one lateral funiculus

tions this is not too clear. In one area in the midthoracic region, there is a focus in which almost complete dissolution of tissue is seen in one lateral funiculus. Macrophages are seen in this area, which would indicate that a cavity is in the process of formation. There is no intrinsic inflammatory activity.

"The process of demyelination appears to be most intense in the thoracolumbar region where it involved the ventrolateral areas and to a lesser degree the gray matter of the ventral horns. The ventral nerve roots are affected with some slight possibility of the dorsal roots also being involved along with the sensory pathways in the lateral funiculi. One might synthesize, therefore, an irregularly segmented motor sensory syndrome with a predominantly lower motor neuron component along with a lateral and ventral spinothalamic syndrome, possibly of irregular distribution and of variable intensity. There is possibly some change in the dorsal column which is difficult to detect and interpret. The etiology is not evident from the sections examined. There is no acute process, the duration of the lesion being measured certainly in terms of months or many weeks. Indeed a few small areas of gliosis seem to confirm the chronic nature of this process."

DISCUSSION

The authors are of the opinion that the cause of the paraplegia in this case was the direct toxic action of the 70 per cent urokon (sodium acetrizoate) on the spinal cord. No definite thrombosis of the anterior spinal artery or its branches could be demonstrated. The pathological examination of the spinal cord revealed a process of demyelinization, which was more intense in the thoracolumbar region and principally involving the ventrolateral areas of the lateral funiculi and most of the ventral funiculus. The nutrient artery supplying this portion of the cord is the anterior spinal artery (i e, anterior radicularis magna).

The blood supply of the spinal cord has been studied by many investigators, particularly Kadyis.[11] The latter demonstrated that the vascular supply of the spinal cord is predominantly of a transverse and segmental nature and that the anterior spinal artery does not exist as one continuous long-reaching blood vessel, but rather is composed of a series or chain of smaller arteries of shorter longitudinal extent. The spinal cord appears to be supplied by six to eight anterior radicular arteries. Their distribution is not symmetrical for there are usually one or two in the lumbar region, one in the lower thoracic region, none or one in the middle thoracic region, one or two in the lower cervical region and one in the upper cervical region. The largest artery is the one found in the lower thoracic or lumbar portion of the cord, which is designated as the "arterial radicularis magnae" by Kadyis. This artery measures 872 microns in diameter in the adult, is single, not symmetrical, and occurs on one side only, usually the left. It is most frequently found in the second lumbar segment, but may be found in any segment between the eighth thoracic and second lumbar.

With the patient in the prone position and the direction of the needle pointing toward the ventral surface of the aorta, one can readily understand how a large stream of highly concentrated medium injected under violent pressure could enter the arteriae radicularis magna and permit the direct toxic action of the drug upon the spinal cord. In this respect it is interesting to note that Hol and Skjervan[12] have performed an interesting experimental study of the causes of spinal cord damage following aortography. They performed abdominal aortography in 18 rabbits by injecting the contrast medium (20 per cent diodrast) through a cannula inserted into the exposed left renal artery. They found that the repeated injections of this high concentration of the contrast medium into the abdominal aorta in rabbits gave rise to toxic damage to the spinal cord as a result of permeation of the spinal arteries by the contrast medium. Spasms and paralysis of the hind parts were encountered. The cord lesions occurred when the animals were injected in the supine position and not in the prone position. It is important to note that the technique and position of the animal employed were not the same as those used in translumbar aortography.

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[11] Kadyis. Quoted by Antoni and Lindgren, loc cit.

There is no unanimity of opinion concerning the pathogenesis of paraplegia in translumbar aortography. Antoni and Lindgren maintained that the lesion was caused by compression of the aorta by the pillow placed beneath the abdomen, thereby supporting Steno's experiment (Niels Stensen 1638–1686) on compression of the abdominal aorta at the level of the renal arteries in rabbits producing motor and sensory paralysis of the lower part of the body. Boyarsky was the first to attribute the paraplegia to the toxic action of the contrast medium on the spinal cord, and the authors concur with this opinion.

Hol and Skjervan have maintained that damage to the spinal cord following translumbar aortography may be expected theoretically under the following circumstances, singly or combined, viz., 1) supine position of the subject, 2) prolonged exposure to the contrast medium, 3) repeated injections of the contrast medium at short intervals, and 4) pre-existing weakness of the arteries of the spinal cord. They pointed out that with the patient in the supine position the high specific gravity of the contrast medium predisposes to the high concentration of the contrast medium with the dorsal arteries supplying the spinal cord. They maintained that this phenomenon is more likely to occur where aortography is performed by the method of retrograde catheterization of the femoral artery wherein filling of the dorsal branches of the aorta as well as the renal arteries occurs. We have failed to observe a single case of filling of the dorsal branches of aorta and the spinal arteries in more than 150 cases of retrograde aortographies. Hol and Skjervan also suggested the possible causative role of prolonged exposure to the contrast medium resulting from retardation of the bloodstream in cases of aortic coarctation, embolus or thrombus formation, reduced blood pressure, abdominal compression and possibly injections too violently performed in a proximal direction.

Little consideration has been given to the likelihood of spinal cord damage being caused by localized ischemia resulting from transient or permanent vasospasm of the dorsal arteries supplying the spinal cord and induced by the velocity of the injection on the direct chemical action of the highly concentrated contrast medium According to Boyarsky, transient vascular spasm has been observed repeatedly following the use of organic iodides, but no case of permanent thrombosis has been reported although such cases have occurred following the use of inorganic (sodium) iodides Goodwin and Walter[13] have successfully employed the intra-aortic injection of 3 to 6 cc of 1 per cent procaine immediately before injecting into the aorta 20 to 30 cc of the contrast medium in order to prevent the brief cramping pains in the abdomen and lower extremities, which are due to transient arterial spasm caused by the irritating effect of the organic iodide contrast medium

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[12] Hol, R. and Skjervan, O.: Acta. radiologica, **42:** 276, 1954.

CONCLUSION

A rare complication of translumbar aortography characterized by sudden onset of paraplegia with areflexia, thermanesthesia, and loss of bladder and rectal control is reported The complication occurred 6 hours after the injection of 70 per cent urokon sodium into the abdominal aorta The procedure was done in the usual manner and all the customary precautions were employed

Although this is the fourth authentic case reported in the literature, the authors are inclined to believe that the true incidence of this complication is greater than these reports indicate

The authors believe that the cause of the paraplegia was the spinal cord changes produced by direct toxic action of the highly concentrated contrast medium which reached the spinal cord through the anterior spinal arteries and its collateral branches The possible etiological role of a transient or permanent vasospasm or thrombosis of the spinal artery cannot be completely excluded despite the fact that no evidence of vasoconstriction or thrombosis was found in the pathological examination of the affected tissue

The authors reaffirm their belief that translumbar aortography is a relatively safe and simple procedure, but its use as a diagnostic procedure must always be carefully evaluated in any given case The possible complications of this procedure must always be borne in mind

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[13] Goodwin, W E and Walter R C Angiography, 4: 410, 1953

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

THE AUTOPSY INCIDENCE OF UREMIA: ITS CLINICAL IMPLICATIONS

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Uremia has long been a well recognized clinical entity. It is known that various diseases of the genitourinary tract and extrarenal factors may play a part in its cause. It is difficult to find the percentage of uremic cases due to such diseases in the standard textbooks or in the recently available literature.[1] Recent advances in understanding of fluid and electrolyte balance and the development of the artificial kidney, as well as the current successful application of more extensive surgical procedures, make it desirable to have more accurate information concerning the incidence of medical and surgical lesions of the genitourinary system which may cause uremia. The knowledge of the exact mechanisms involved and which of these may be reversible by medical and surgical therapy should be reevaluated in view of current trends in medicine and surgery.

MATERIAL AND METHODS

In order to further study the problem of uremia, a series of 8002 consecutive cases autopsied at the Queens General Hospital from 1935 to 1949 inclusive were reviewed. Four hundred and seventy-eight (6 per cent) of these were considered to be examples of uremia and were selected according to the following criteria. In most of these cases the prosector considered that uremia was present clin ically and pathologically; these records showed confirmatory evidence clinica (e.g., elevated blood urea nitrogen, uremic frost, etc.) and pathologically (e. characteristic lesions in the pericardium, colon, pancreas, lungs, etc.), and morphological changes were recent; there were no other factors sufficie themselves to explain these clinical and/or pathological findings. In some cases selected for this study the prosector did not state that uremia was but a review of all the clinical and the pathologic findings in the p severe and extensive renal lesion made this diagnosis inescapable. Only the cases included in the present series showed clinical and corroborative logical evidence of uremia in the absence of severe lesions in the ki elsewhere in the genitourinary system.

The following groups of cases did not meet the aforementioned criteria therefore not included in the present study: 1) Any severe renal or p lesion in which the clinical course was too acute to permit adequate w uremia (e.g., blood urea nitrogen was not performed) and in which the clearcut corroborative evidence of uremia morphologically (e.g., urem ditis, uremic penumonitis, uremic changes in the pancreas). 2) Also excl

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Accepted for publication September 21, 1955.

[1] a) Bell, E. T.: Renal Diseases. Philadelphia: Lea and Febiger, 1950.
b) Herbut, P. A.: Urological Pathology. Philadelphia: Lea & Febiger, 1952.
c) Anderson, W. A. D.: Pathology. St. Louis: C. V. Mosby, 1953.

TABLE 1. *Cause of uremia in 478 cases*

	per cent
Cancer..	15
Post-renal and infection	39
Benign nephrosclerosis	13
Glomerulonephritis	11.5
Malignant nephrosclerosis	7.3
Combined causes	
Post-renal and infection with others	9.8
Nephrosclerosis with others .	9 6

those cases in which clinical and pathological findings did not substantiate a diagnosis of uremia made by the clinician.

The constant degree of uniformity in the evaluation and categorization of these cases is worth emphasizing since the gross organs, the microscopic sections and the classification of each case were reviewed by one of the authors (A. A. A.) within one or two weeks of the time that the autopsy was performed.

However it should be understood that a certain amount of personal judgment is necessary because of the loose definition of uremia which makes it difficult to differentiate from a terminal uremic-like state or azotemia in some instances. Thus a patient may die with evidence of uremia but not because of uremia. From a study of the genitourinary system alone, it is ordinarily not possible to evaluate the severity or duration of uremia.

The present study is limited to the morphologic aspects, and no discussion is attempted of the biochemical, endocrine, or other mechanisms involved.

The most frequent causes of uremia are listed in table 1. Some cases had more than one renal lesion, and therefore are included in several categories. The total percentages given in the tabulation would thus exceed 100 per cent, even though several smaller miscellaneous groups are not tabulated.

RESULTS AND COMMENT

Uremia, as defined here, occurred in 6 per cent of 8,002 consecutive autopsied cases at a large general municipal hospital from 1935 to 1949, inclusive.

Cancer was responsible for 15 per cent of all of the cases of uremia. These were usually instances of pelvic carcinoma which resulted in obstruction of the urinary system, most often with associated infection. Since most of these carcinomas originated in the prostate, bladder or uterus, the older age groups were most affected. This group will attain greater significance because of the increasing proportion of the population in the susceptible age periods. Because of the much greater frequency of carcinoma of the prostate, the ratio of men to women in this group was more than 4 to 1. Uremia due to replacement of the renal parenchyma itself by tumor is exceedingly rare.[2]

Instances of urinary tract obstruction and infection not due to carcinoma of the genitourinary system account for 39 per cent of all cases of uremia. In an

[2] Wallach, J. B , Scharfman, W B. and Angrist, A. A.: J. Urol., **67**: 623, 1952.

THE JOURNAL OF UROLOGY
Vol. 75, No. 2, February 1956
Printed in U.S.A.

CLEARANCE WITHOUT PROLONGED INFUSION, WITH ONLY ONE CLEARANCE PERIOD, A NEW CLEARANCE FORMULA, AND WITHOUT A CATHETER

HANS CLAUSEN

The tests which have resulted in a different clearance method were carried out with PAH clearance (C_{PAH})*, but they also apply analogously to inulin clearance (C_{In}) and every corresponding method. In addition, these new results also permit corresponding conclusions with respect to all subsequent formulae which contain C_{PAH} and C_{In}. Only $T_{m\text{PAH}}$ and $T_{m\text{Glucose}}$ and analogous methods actually have a certain independence.

When changing the clearance it was our aim, first, to stabilize the results, and also the normal values, and second, to simplify the method for the patient, the physician and the laboratory.

We inject the test substance only once in most cases, 3.0 gm. mostly being sufficient in the case of PAH. Where, contrary to expectation, almost everything has been discharged in the second hour we recommend a repetition, during which a quantity of 2 gm. of PAH is subsequently injected in the thirtieth minute. But this will only happen here and there in the case of young, healthy persons. Whoever wishes to adhere to prolonged infusion may do so, but he should discontinue the same some 10 minutes before the beginning of the clearance examination. Prolonged infusion should not disturb the clearance. Full information on this subject will be found in one of our other publications in the *Medizinische Monatsschrift.* The only possible advantage might be to apply high doses of the test substance in a very careful and creeping-in manner. For the principle of the clearance methods prolonged infusion is dispensable and even a hindrance. Where a great delay in discharging is to be expected, only up to 1 gm. of PAH may be given. After application it will suffice to carry out only one clearance period if 4 conditions are fulfilled, namely: 1) Clearance must be carried out between the sixty-fifth and ninety-fifth minute. 2) The patient must remain lying in the dorsal position and must not move. 3) No medicines should have previously been administered which might have a disturbing influence. 4) The cannulas must be kept free from test substance. 5) It is recommended to then carry out clearance by the following formula:

$$\text{Clearance} = \frac{U \cdot V}{\dfrac{(P_1 - P_2) \cdot \log e}{(\log P_1 - (\log P_2)}}$$

Under these conditions it will even be possible to work with spontaneous urine, the only difference being that point 1 above will have to be changed in that the

---

Accepted for publication July 29, 1954.

* We used the sodium salt of p-amino hippuric acid which is marketed under the name of "nephrotest" by Cassella Farbwerke Mainkur Aktiengesellschaft, Frankfurt (Main) Fechenheim, Germany. This preparation has proved to be well tolerated, gives precise clearance results and also proves to be very reliable also in the analytical determination according to the method of Bratton and Marshall (J. Biol. Chem., **128**: 537, 1939).

clearance period is extended beyond the ninety-fifth minute. However, working with spontaneous urine entails a number of further sources of error. It is therefore recommended to wait, before evaluating the results with spontaneous urine, until all other factors which influence clearance, have been very carefully studied with the catheter method.

P should not be calculated from the mean time of two values, and *P* should also not be measured only once in the middle of the clearance period. It would require a lengthy explanation why that would lead to incorrect results for physiological and mathematical reasons. We shall therefore revert to this matter in a later publication. In the field of clearance there remain a large number of questions to be clarified, and the question of dosage of the test substance is one of them. There are still some points which I myself do not yet fully understand. It would require a large series of very cumbersome tests to find a solution to all these questions. I already have a plan before me for the manner in which these tests should be carried out.

The most interesting results are undoubtedly to be expected from the further research work with respect to the kinetics of concentrations in the body fluids. We ourselves shall shortly make a contribution to this subject in the English literature.

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South Central—Mexico City, Hotel Del Prado, October 28-31, November 1, 1956
Southeastern—Hollywood Beach, Fla., March 25-29, 1956
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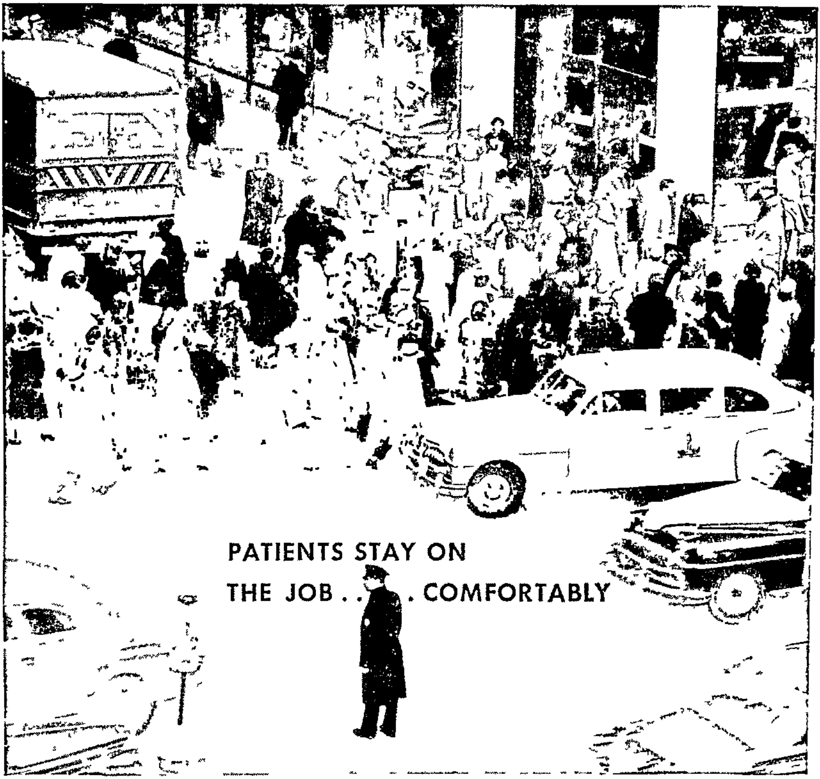
Note by editor. A complete list of the executive committees of the various sections, and a complete list of the officers and members of the executive committees of the various branch societies was printed in the December 1955 issue.



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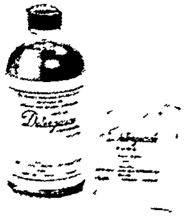

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*Lattimer, John K., and Spirito, A. L.; Clorpactin for Tuberculous Cystitis. Journal of Urology, Vol. 73, June, '55.

Wolinsky, E., Smith, M. M., Steenken, W., Jr; Tuberculocidal Activity of Clorpactin, a new Chlorine Compound. Antibiotic Medicine Vol. I No. 7 July, '55.

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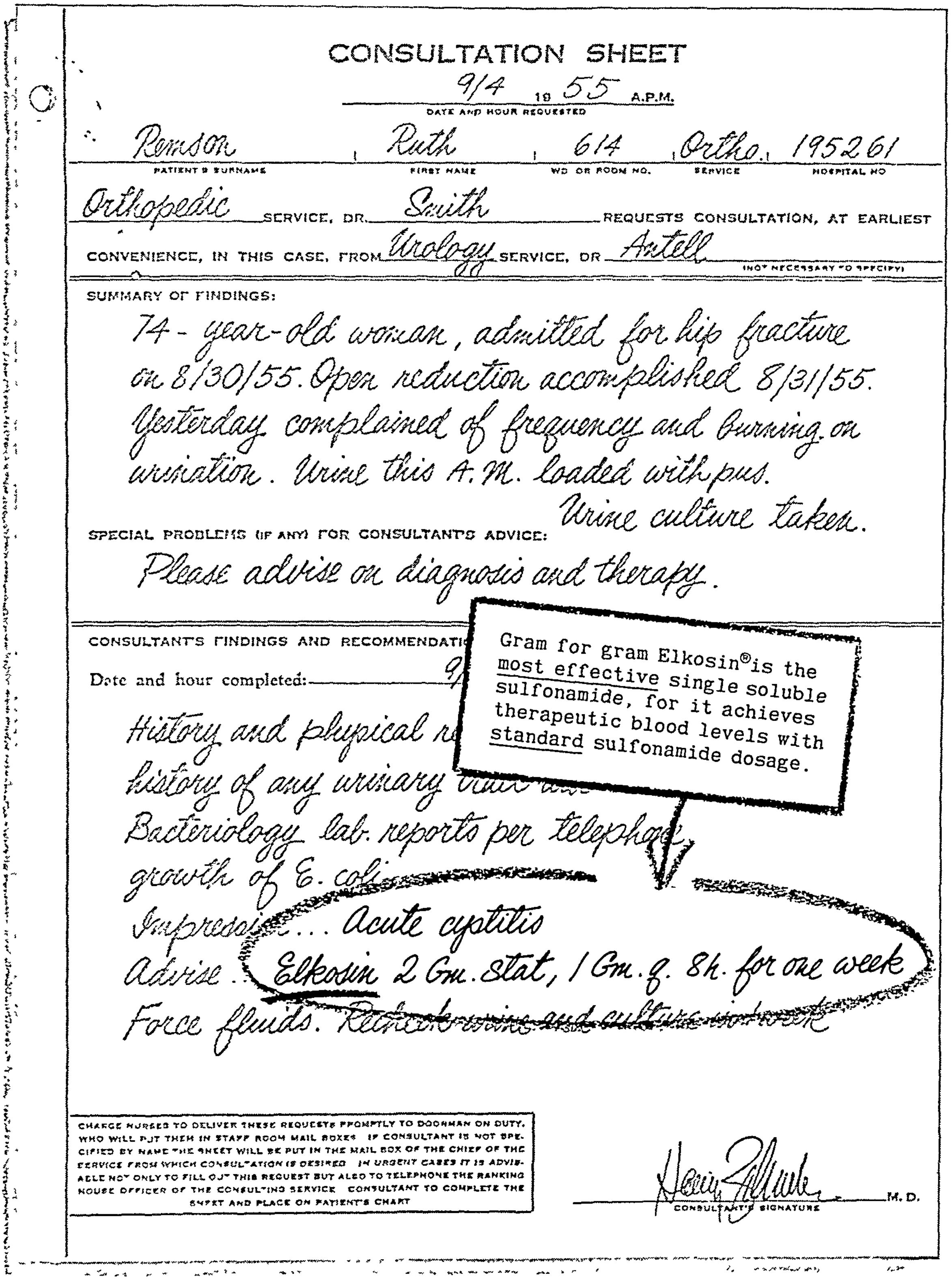

CONSULTATION SHEET

9/4 19 55 A.P.M.
DATE AND HOUR REQUESTED

Remson	Ruth	614	Ortho.	195261
PATIENT'S SURNAME	FIRST NAME	WD OR ROOM NO.	SERVICE	HOSPITAL NO

Orthopedic SERVICE, DR. Smith REQUESTS CONSULTATION, AT EARLIEST CONVENIENCE, IN THIS CASE, FROM Urology SERVICE, DR Antell (NOT NECESSARY TO SPECIFY)

SUMMARY OF FINDINGS:

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SPECIAL PROBLEMS (IF ANY) FOR CONSULTANT'S ADVICE:

Please advise on diagnosis and therapy.

CONSULTANT'S FINDINGS AND RECOMMENDATI

Date and hour completed: 9/

History and physical re
history of any urinary trac
Bacteriology lab. reports per telephone
growth of E. coli
Impression... Acute cystitis
Advise... Elkosin 2 Gm. stat, 1 Gm. q. 8h. for one week
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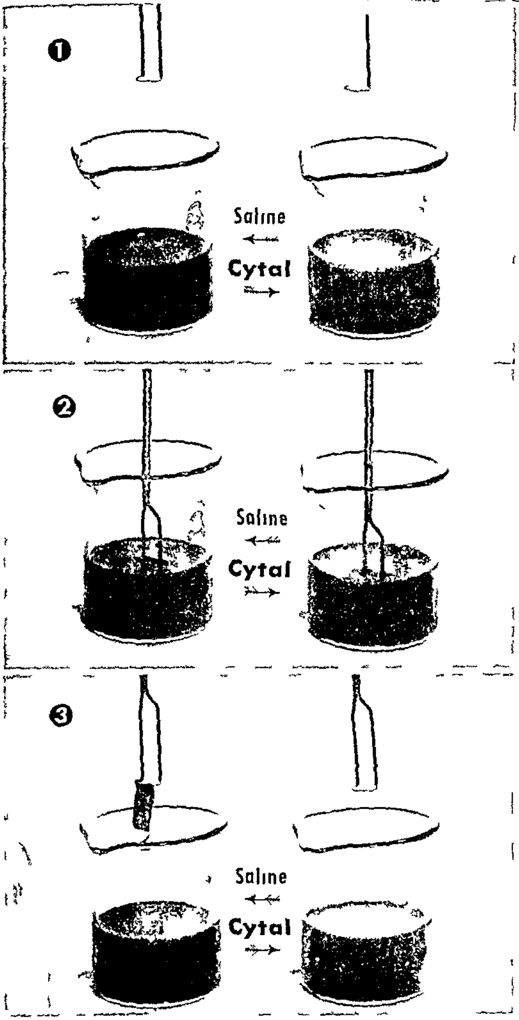

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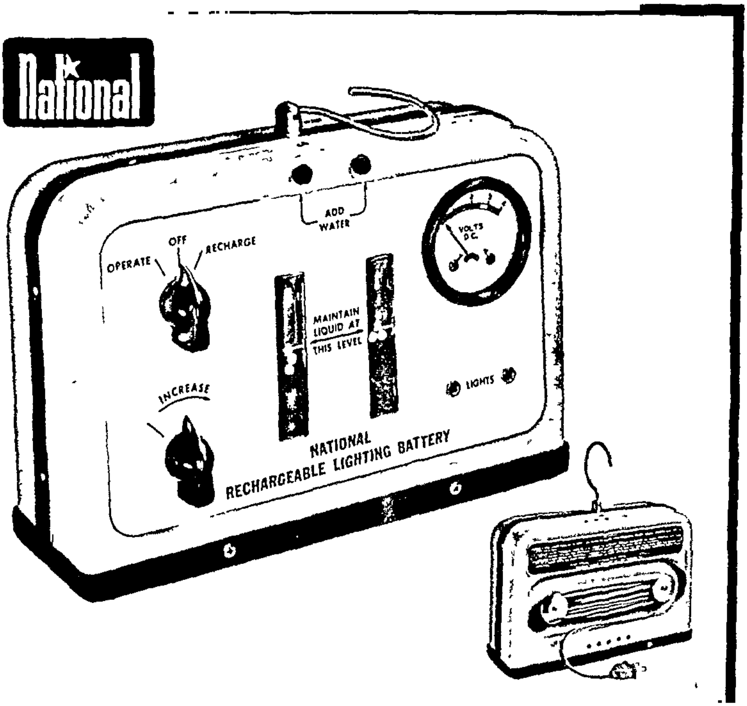
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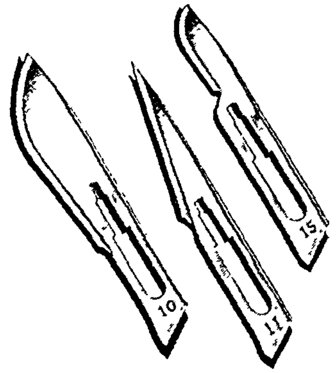

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(Contents continued from front cover)

Sclerosing Lipogranulomas of Male Genitalia. *A. R. Marcial-Rojas, J. E. Colon and J. J. Figueroa* 334
Response of Urinary Tract Infections Treated by Elkosin, Gantrisin, Triple Sulfa or Triple Sulfa-Achromycin. *W. E. Clapper and L. E. Plank* 339
Acute Urinary Retention due to Drugs. *S. J. Schneierson and Harry Bergman* 342
Paraplegia, a Rare Complication of Translumbar Aortography. *B. S. Abeshouse and A. T. Tiongson* 348
Autospy Incidence of Uremia. *J. B. Wallach, Macellis Glass and A. A. Angrist* 356
Clearance Speed: A New Clearance Method. *Hans Clausen* 361
Clearance Without Prolonged Infusion. *Hans Clausen* 364

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CONTENTS

Plastic Repair of Hydronephrosis. *J. S. Gardner* 367
Current Status of Chemotherapy of Renal Tuberculosis. *J. K. Lattimer and A. L. Spirito* 375
Aneurysm of Renal Artery. *R. M. Nesbit and W. B. Crenshaw* 380
Pathology of Tumors of Renal Pelvis and Ureter. *J. T. MacLean and V. B. Fowler* 384
Diagnosis of Tumors of Renal Pelvis and Ureter. *V. J. O'Conor* 416
Prognosis of Primary Tumors of Renal Pelvis and Ureter *J. E. Dees* 419
Localized Amyloidosis of Ureter *D. R. Higbee and W. D. Millett* 424
Smooth Muscle Regeneration in Repair of Experimental Ureteral Defects. *Frank Hinman, Jr. and Rudolf Oppenheimer* 428
Diagnosis of Urologic Complications in Gynecology. *Carl Rusche* 433
Treatment of Urologic Complications in Gynecology. *Edgar Burns and Irving Peiser* 438
Is Cystitis Cystica an Innocent or a Malefic Lesion? *R. M. Nesbit* 443
Exstrophy of Bladder: Treatment by Plastic Surgery *T. H. Sweetser, T. C. Chisholm, W. H. Thompson, E. B. Berglund, S. P. Wesolowski and T. H. Sweetser, Jr* 448
Partial Cystectomy for Hypotonic Bladder. *C. D. Creevy* 456
Atonic Neurogenic Bladder in Porphyria. A. G. Redeker 465
Ileal Loop Diversion: Its Application to Treatment of Neurogenic Bladder Dysfunction. *W. F. Leadbetter and F. G. Shaffer* 470
Study of 2678 Patients with Initial Carcinoma of Bladder I. Survival Rates. *F. K. Mostofi* 480
Study of 2678 Patients with Initial Carcinoma of Bladder II. Survival Rates in Relation to Therapy. *F. K. Mostofi* 492
Radical Operation for Cure of Intractable Stricture of Male Urethra. *A. B. Cecil* 501
Carcinoma of Male and Female Urethra: Pathology and Diagnosis. *A. L. Dean* 505
Treatment of Urethral Tumors *R. H. Flocks* 514
Effect of Cortisone on Spermatogenic Function of Human Testes J. H. McDonald and N. J. Heckel 527
Dependent Drainage Via Perineum in Retropubic Prostatectomy. *Richard Chute and E. F. Ireland, Jr.* 530

(Contents continued on page 38)

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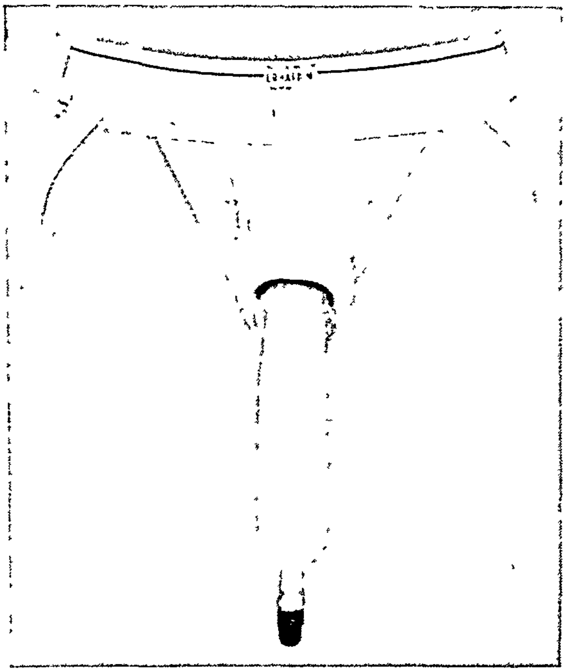

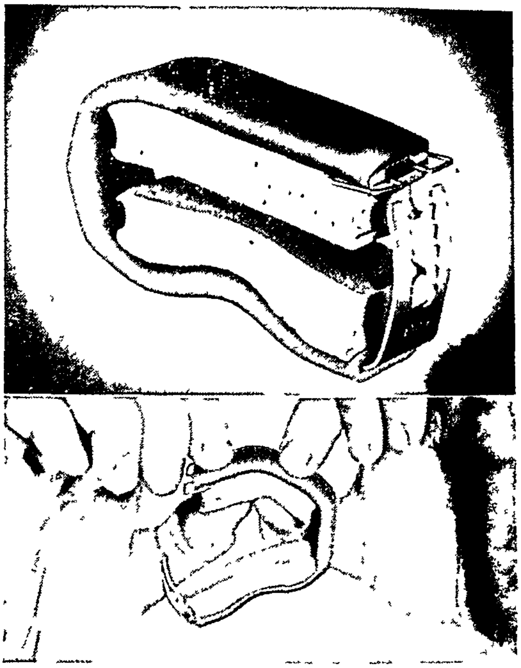

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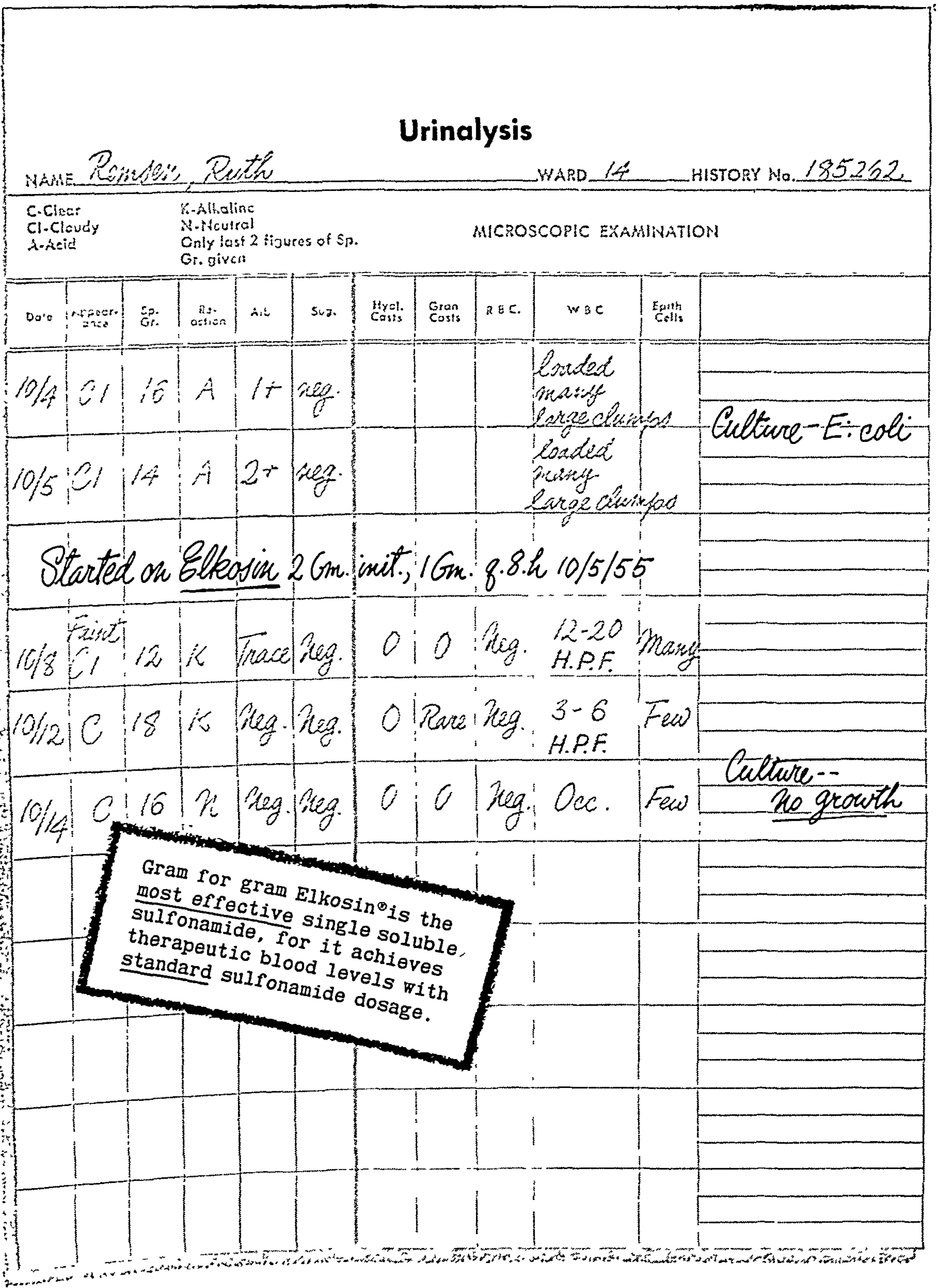

Urinalysis

NAME Romber, Ruth WARD 14 HISTORY No. 185262

C-Clear
Cl-Cloudy
A-Acid

K-Alkaline
N-Neutral
Only last 2 figures of Sp. Gr. given

MICROSCOPIC EXAMINATION

Date	Appearance	Sp. Gr.	Reaction	Alb.	Sug.	Hyal. Casts	Gran Casts	R B C.	W B C	Epith Cells	
10/4	Cl	16	A	1+	neg.				loaded many large clumps		Culture-E. coli
10/5	Cl	14	A	2+	neg.				loaded many large clumps		
Started on Elkosin 2 Gm. init., 1 Gm. q.8.h 10/5/55											
10/8	Faint Cl	12	K	Trace	Neg.	0	0	Neg.	12-20 H.P.F.	Many	
10/12	C	18	K	Neg.	Neg.	0	Rare	Neg.	3-6 H.P.F.	Few	
10/14	C	16	N	Neg.	Neg.	0	0	Neg.	Occ.	Few	Culture-- No growth

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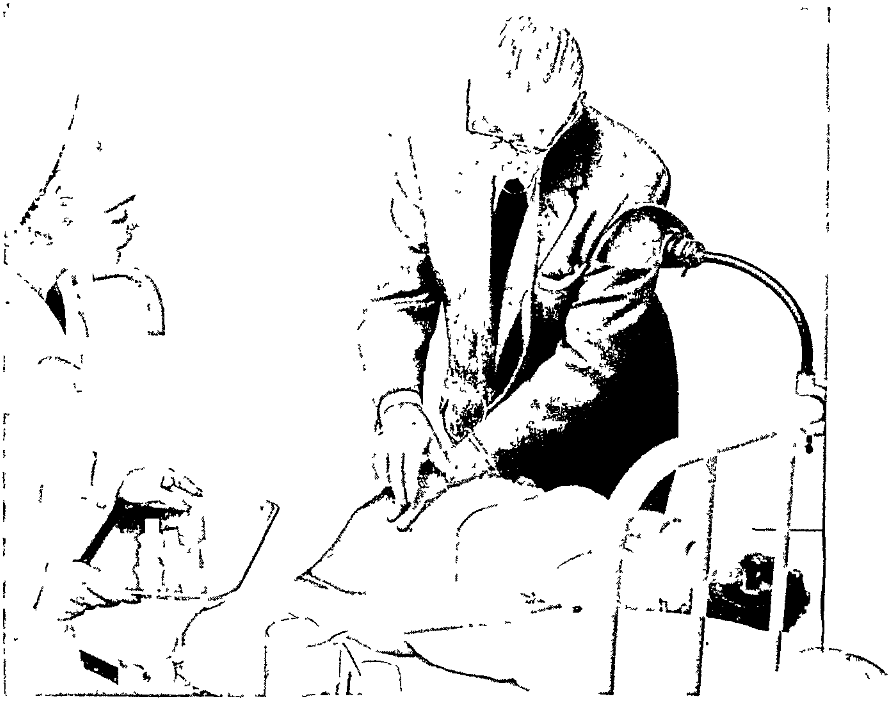

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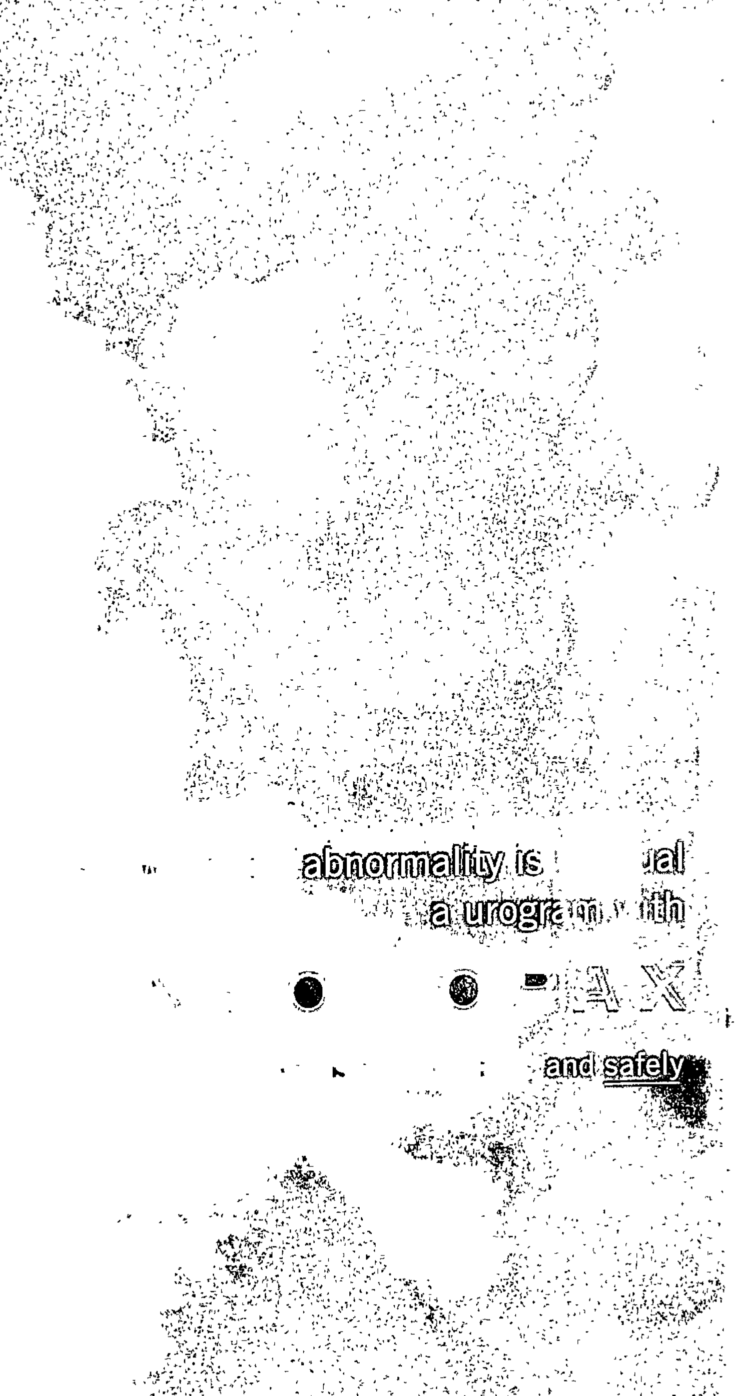

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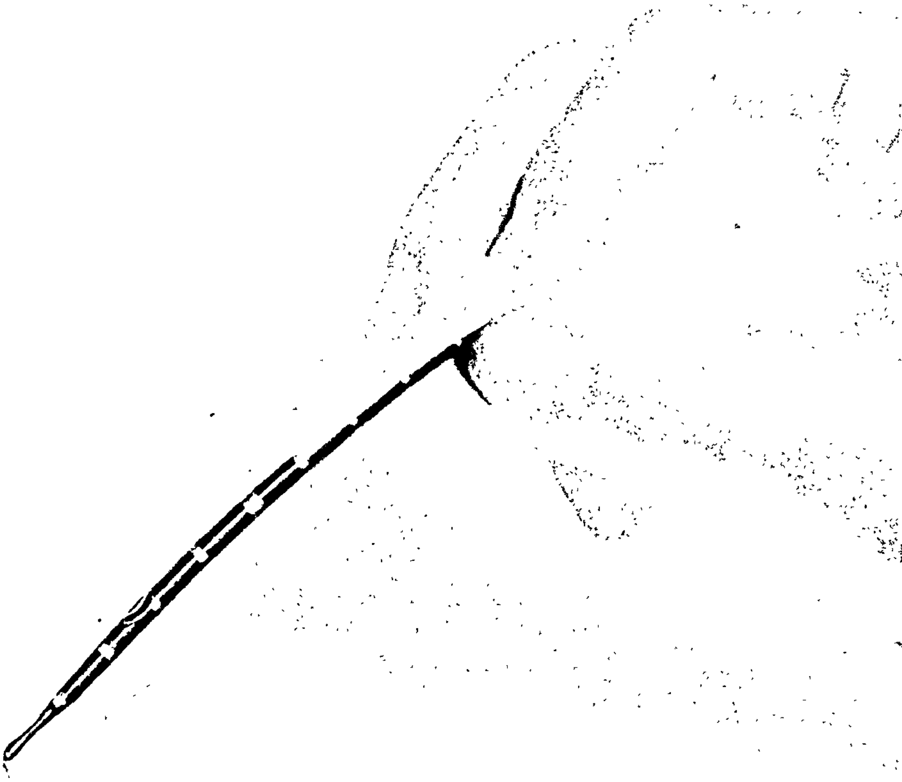

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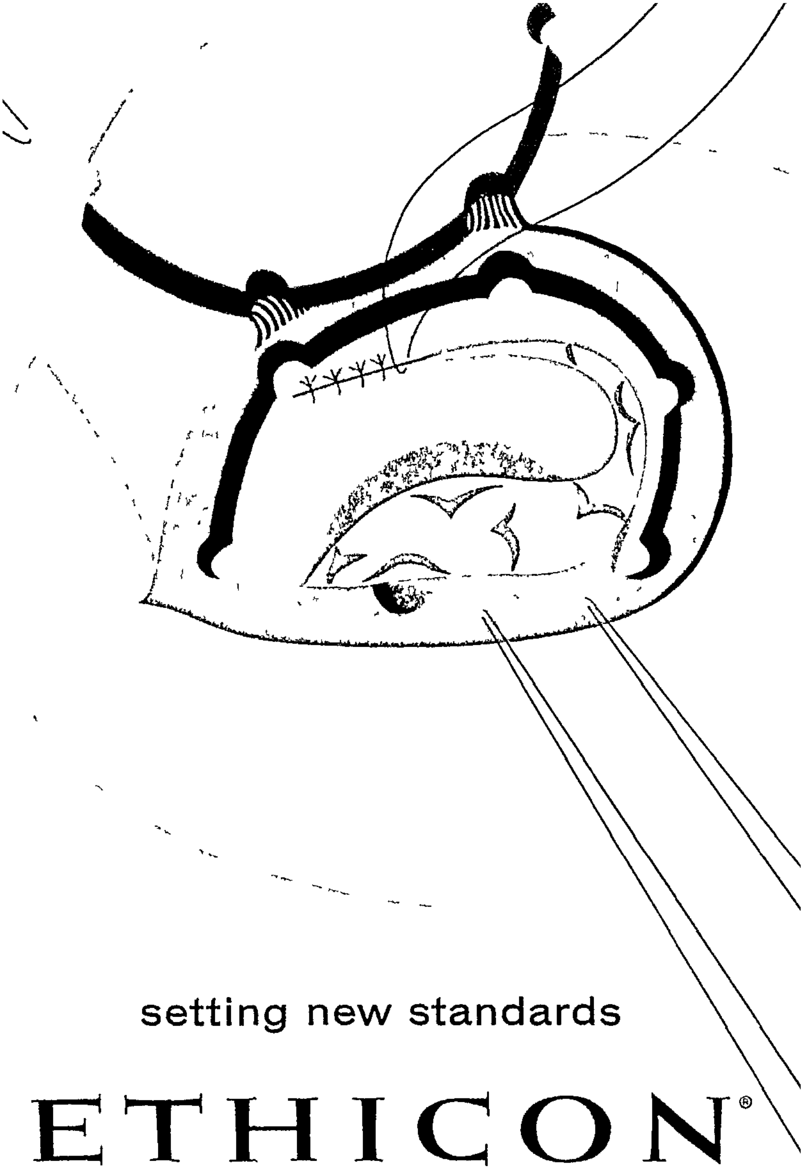

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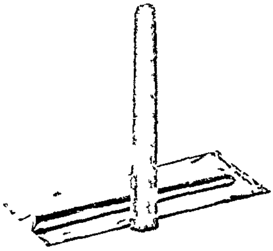

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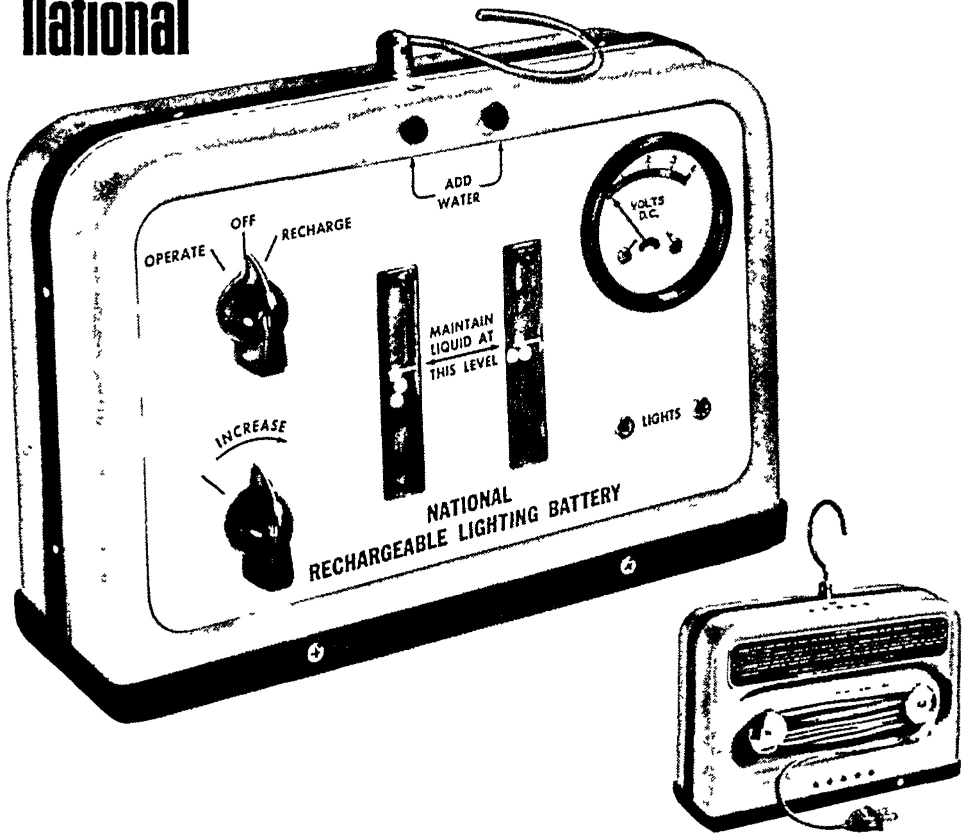

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[1] O'Conor, Vincent J.; Clorpactin WCS-90 in the treatment of interstitial cystitis. *Quarterly Bulletin* Northwestern Univ. Med. School, Chic., 1955, Vol. 29, No. 4, Page 392, Winter Quarter.

[2] Lattimer, John K. and Spirito, A. L.; Clorpactin for Tuberculous Cystitis. Journal of Urology, Vol. 73, June, '55.

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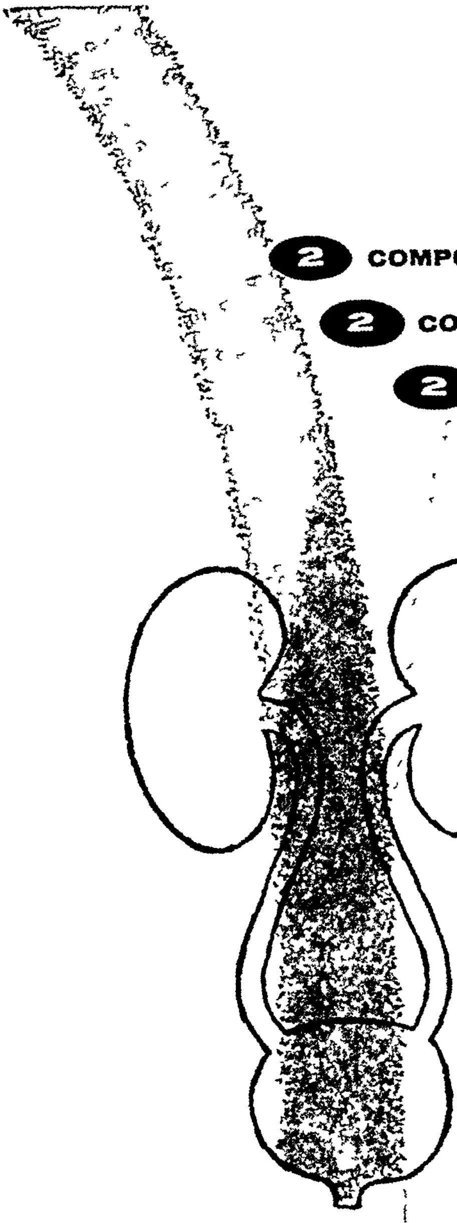

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[1] a) Nicolai C H MIOKON A Preliminary Clinical Report on a New Intravenous Urographic Medium Missouri Medicine 52 703 (Sept 1955)

b) Nicolai C H *(Private Report dated July 19, 1955 on 1138 cases)*

c) Nicolai C H MIOKON a New Intravenous Urographic Medium (To be published J Urol)

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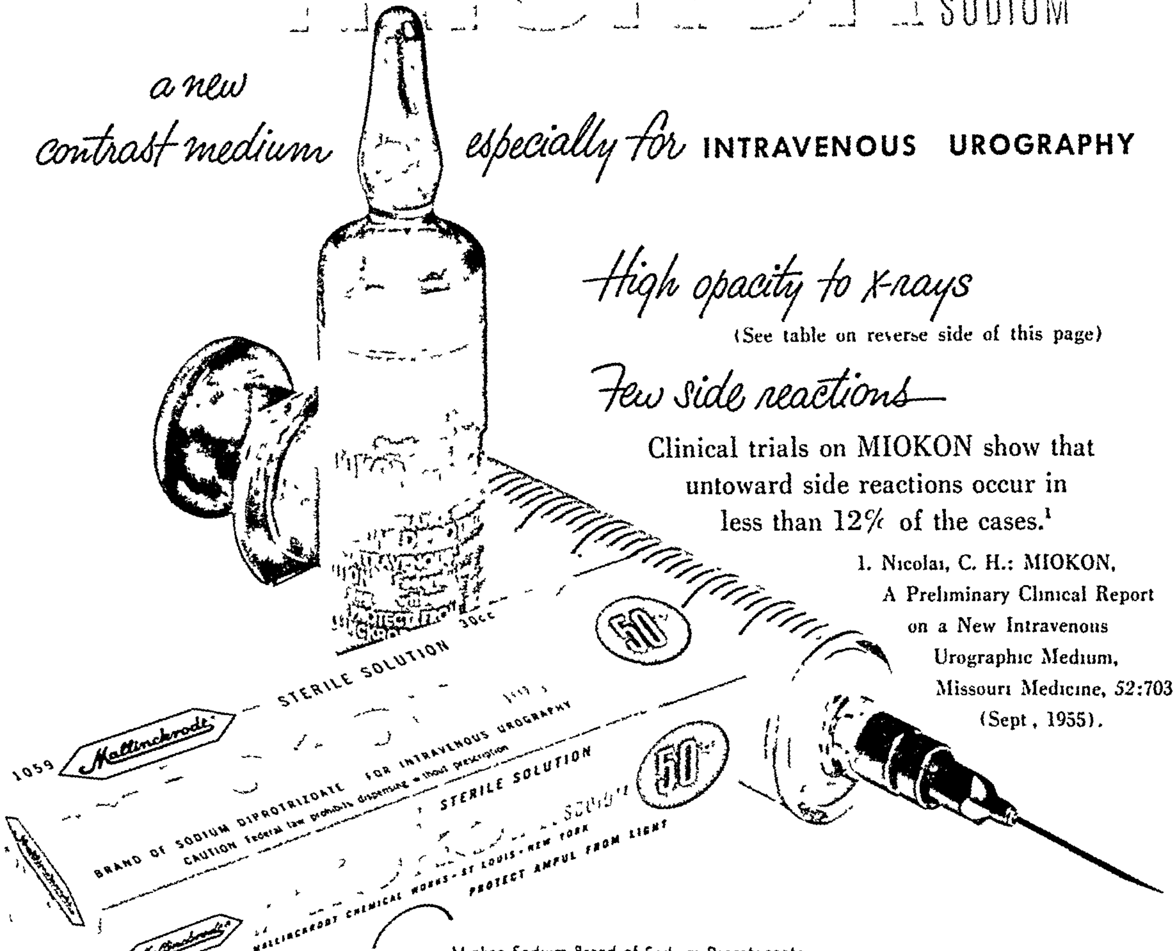
[1] Nicolai, C. H.: MIOKON, A Preliminary Clinical Report on a New Intravenous Urographic Medium, Missouri Medicine, *52*:703 (Sept., 1955).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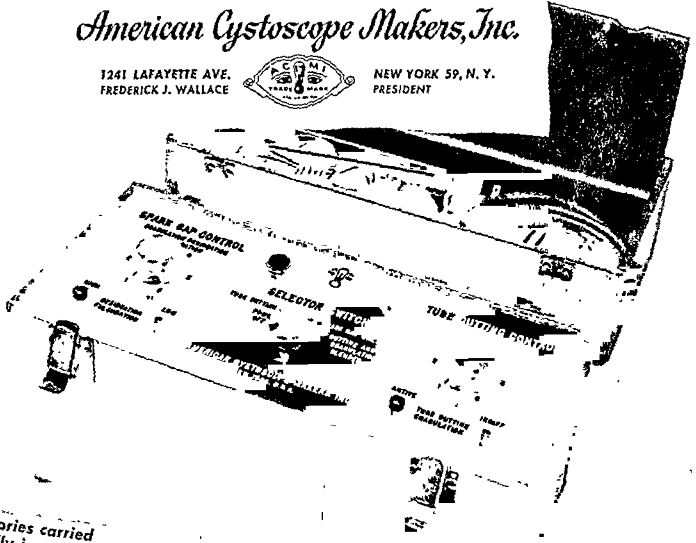

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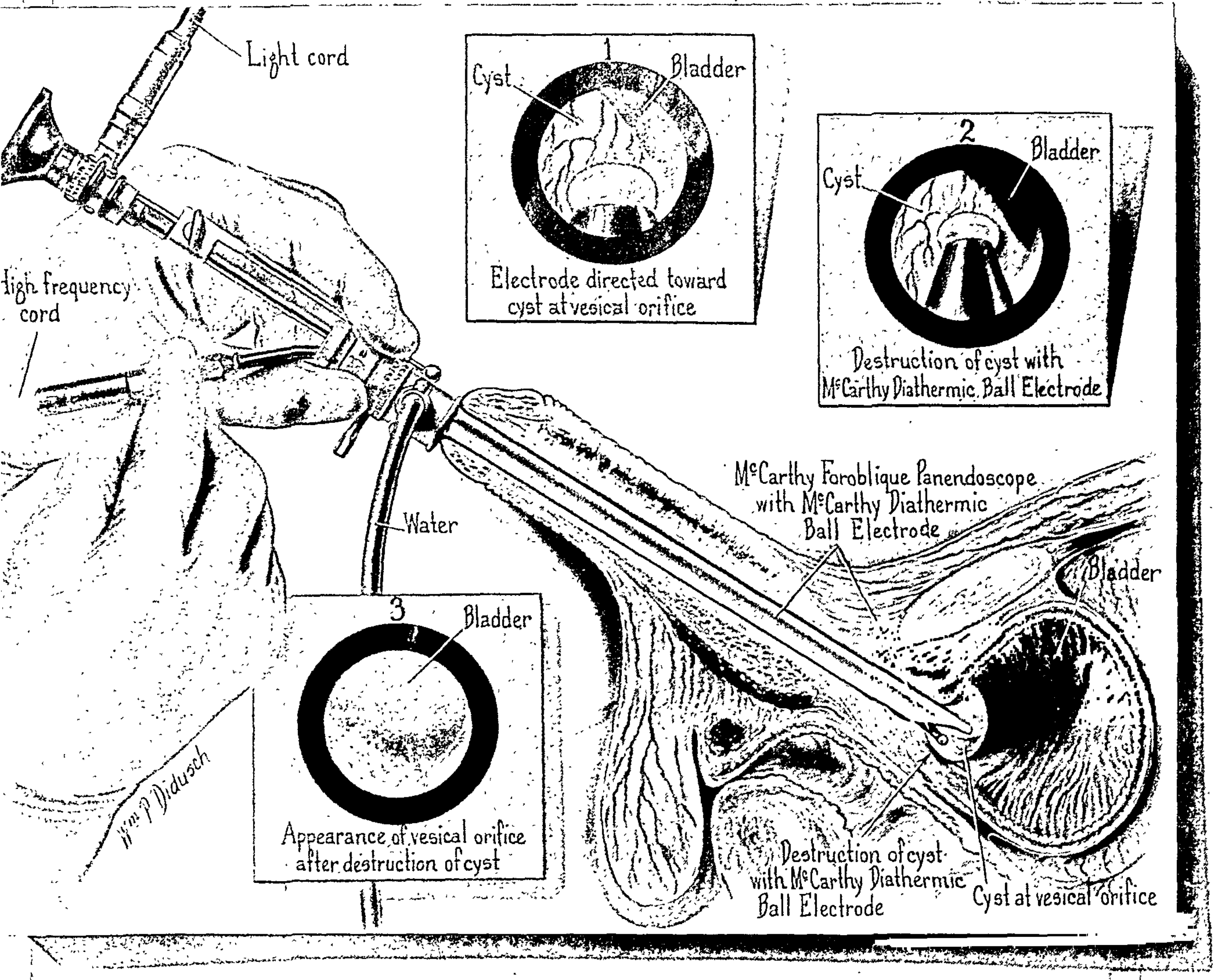
Light cord
High frequency cord
Water
1
Cyst
Bladder
Electrode directed toward cyst at vesical orifice
2
Bladder
Cyst
Destruction of cyst with McCarthy Diathermic Ball Electrode
3
Bladder
Appearance of vesical orifice after destruction of cyst
McCarthy Foroblique Panendoscope with McCarthy Diathermic Ball Electrode
Bladder
Destruction of cyst with McCarthy Diathermic Ball Electrode
Cyst at vesical orifice
Wm P Didusch

The illustration above shows the successive steps in the destruction of a cyst at the vesical orifice with the McCarthy Diathermic Ball Electrode passed through the McCarthy Foroblique Pan-endoscope, using a high frequency current.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

PLASTIC REPAIR OF HYDRONEPHROSIS: DESCRIPTION OF NEW TECHNIQUE USED IN 10 CASES

J. SCOTT GARDNER

The value of surgical correction of hydronephrosis is now well established. During the past 65 years many kidneys in serious danger of destruction have been salvaged to carry on years of useful work. Unfortunately, not all attempts to save these hydronephrotic kidneys are successful, a failure rate of 21 per cent having been reported. A new technique is presented because it has enabled the author to avoid secondary stricture, as well as some of the other common causes of failure. This new technique, while utilizing established principles in common with well-known and tried methods, has features of its own which are particularly applicable when the extrarenal pelvis is greatly dilated.

OPERATIVE TECHNIQUE

With the patient lying on the side over a flexed table, a subcostal incision is made of adequate length to insure good exposure of the lower half of the kidney. The ureter is located by opening Gerota's fascia on its posterior surface near the vertebral column. It is traced cephalad to its attachment to the renal pelvis, care being taken to avoid freeing it from its surrounding connective tissue. Exposure is facilitated by retracting the lower pole of the kidney laterally. The lower surface of the hydronephrotic sac then faces the operator. At this point a decision as to the necessity of plastic repair can be made; lysis of adhesions and kinks, or division of small aberrant vessels may allow adequate drainage. If not, some form of plastic repair must be carried out. An incision is made beginning at the ureteropelvic junction and extending toward the lower end of the renal hilus on the anterior surface (fig. 1, *1*). The interior of the pelvis can then be inspected and the ureteral stoma calibrated (fig. 1, *2*). From then on further dissection can be done from inside the pelvis, thus averting the necessity of freeing the external connective tissue and blood supply. Any one of a number of well known plastic procedures can be applied at this point, as indicated. If the pelvis is greatly dilated and reduction of its size appears necessary, a second incision is made from the ureteropelvic junction to the renal hilus on the posterior surface. This should be at an angle of 60 degrees with the first. A V flap is thus made, with its base attached to the lower edge of the renal hilus (fig. 1, *3*). It may be necessary at times to place the V flap either anteriorly or posteriorly in order to move the new ureteral stoma away from an aberrant vessel. The ureter is separated from the pelvis by an incision circumscribing the pelvis 2 cm. proximal to the ureteropelvic junction (fig. 1, *4*). Then beginning at the base of the V flap a parallel incision is made around the cephalad portion of the pelvis at the renal hilus. Thus a large segment of excess tissue is removed (fig. 1, *5*). The V-flap can then be trimmed to the desired size; it should not be more than 3 cm. in length. The ureter is split from the ureteropelvic junction sufficient distance to make it fit the cut end of

Accepted for publication September 21, 1955.

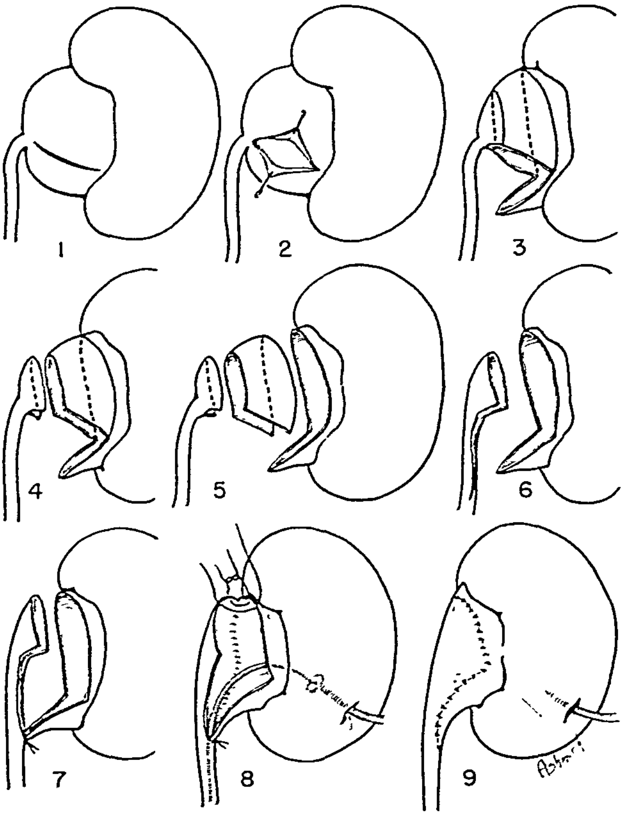

FIG 1

the pelvis and flap, usually 2–3 cm. (fig. 1, *6*). The tip of the V-flap is sutured to the ureter at the lowest end of the split (fig. 1, *7*) with a single 00000 chromic suture. Tissue hooks are used to hold the parts in place while the posterior edges are brought together with interrupted 00000 chromic sutures (fig. 1, *8*). At this point a nephrostomy tube with ureteral splint can be advantageously placed and the closure completed (fig. 1, *9*). The kidney and ureter are placed back into the normal position, a Penrose drain is placed near the repair site and Gerota's fascia is brought around to cover the posterior surface, and sutured in place. The Penrose drain and nephrostomy are brought out the flank wound and the wound closed.

Postoperatively the Penrose drain can usually be removed on or after the sixth day. The nephrostomy tube and ureteral splint should be left in place 14 days longer, as indicated, and following removal, urinary drainage from the sinus should stop within 24 hours. Prompt closure indicates free drainage down the ureter.

Illustrative cases are depicted in figures 2 to 7.

DISCUSSION

No one operative technique is suitable for the repair of all types of hydronephrosis. The plastic repair selected should be suited to the particular defect,

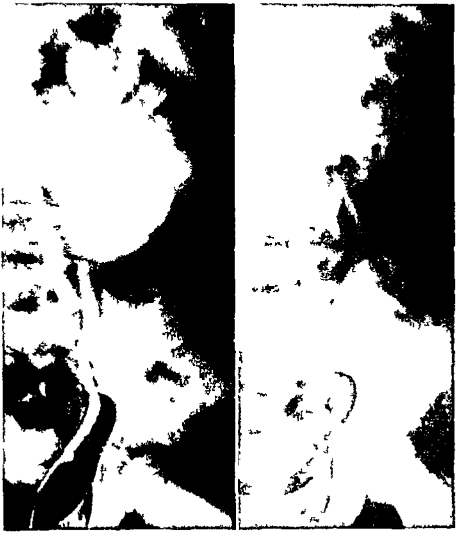

Fig 2 Case 2 W G, boy aged 4 Preoperative retrograde pyelogram and excretory urogram 4 months postoperatively

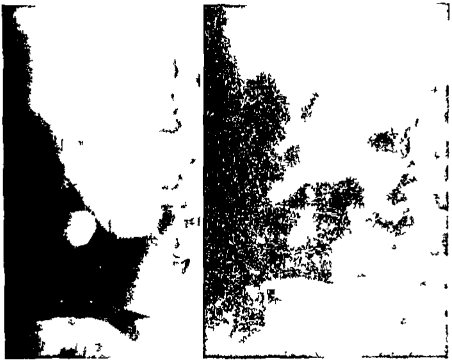

Fig 3 Case 5 M P woman aged 35 Preoperative retrograde pyelogram Excretory urogram almost 7 years later

which can not be completely known until after the surgical exposure It is therefore imperative, when approaching such a problem, that the surgeon be armed with many ideas, both regarding the primary intent and satisfactory alternatives The operation described above may add one more possibility to the urologist's armamentarium

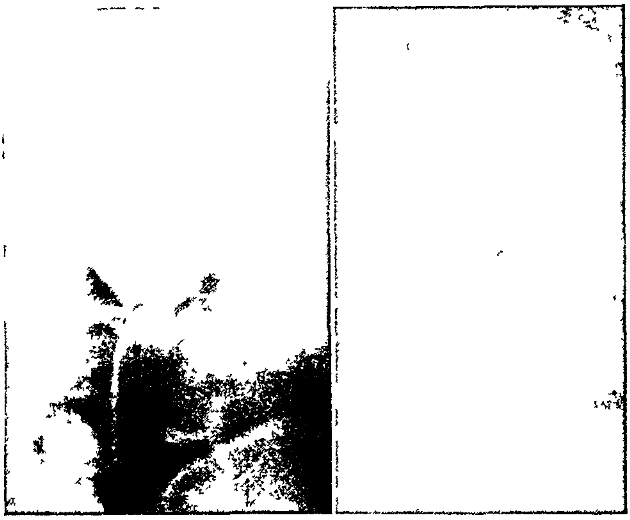

Fig. 4. Case 6. W. M., man aged 45. Preoperative retrograde pyelogram and retrograde pyelogram 2 months after pyeloplasty.

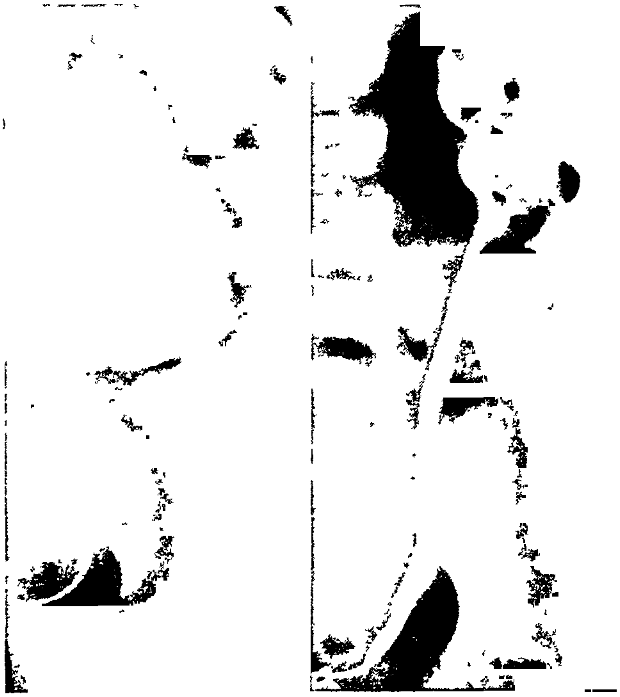

Fig. 5. Case 7. P. R., a baby girl aged 23 months. Preoperative retrograde pyelogram. Retrograde pyelogram 3 years, 3 months later.

The requirements for successful plastic procedures on the ureter and pelvis which have been utilized in the operation may be listed as follows: 1) preservation of adequate blood supply; 2) avoidance of circular suture line; 3) absence of tension and pressure of the suture line; 4) prevention of postoperative distention; 5) ureteral intubation; 6) prevention of infection.

The operation is designed to avoid certain circumstances found in unsatis-

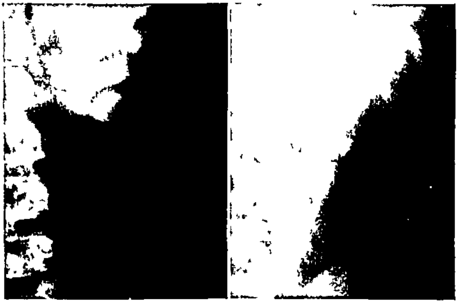

FIG 6. Case S. H. F., boy aged 6 years. Preoperative excretory urogram. Preoperative retrograde pyelography showed no dilatation of ureter from renal pelvis down. Excretory urogram 3 years after pyeloplasty.

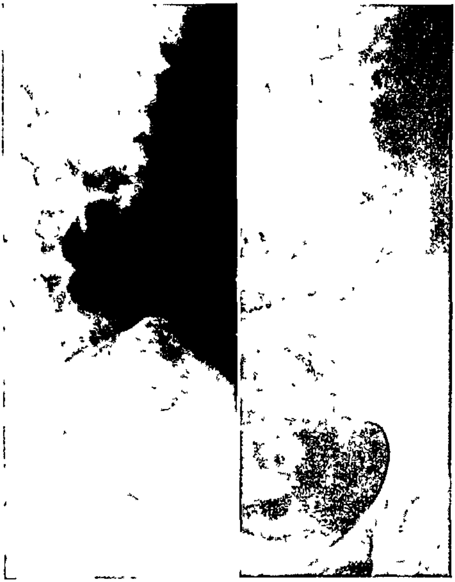

FIG. 7. Case 19 A D., woman aged 34 Preoperative excretory urograms. Excretory urograms 1 year after operation

factory results, which are: 1) insufficient reduction in the size of the enlarged pelvis; 2) irregularities in shape of the reconstructed pelvis; 3) secondary stricture formation; 4) damaged and inadequate blood supply; 5) fibrosis and scarring in and about the operative site.

Preservation of blood supply, imperative in any plastic procedure, can be

Table 1

Patient	Date	Age	Relief of Pain	Nephrostomy No. Days	Urine Leakage Through Sinus No. Days	Duration of Pyuria	Recurrent Pyuria	Pyelographic Improvement
M. H.	4/18/46	44	3 yrs.	29	none	No pyuria 8 mos.	After 3 yrs.	fair
W. G.	6/26/48	4	Permanent	13	none	No pyuria 6 mos.	none	good
M. P.	3/25/48	30	Permanent	18	none	No pyuria 3 mos.	none	good
E. R.	6/21/48 8/3/48	38	2 wks.	9	none until 17th p.o. day	6 wks.; ended with nephrectomy	none	none
S. P.	8/11/49	13	Brief pyelonephritis after 3 yrs.	18	2 dys.	No pyuria 4 mos.	Brief attack after 3 yrs.	good
W. M.	1/7/50 1/18/50	45	Permanent	18	none	No pyuria 7 mos.	none	good
P. R.	3/22/50 8/28/50	23 mos.	Permanent	19	none	No pyuria 5 mos.	Pyuria for 6 wks. after 3 yrs.	good
H. F.	8/17/51 4/18/52	6	Permanent	14	none	No pyuria 70 dys.	Stone at 7 mos.	good
P. M.	12/19/51	2 wks.	Permanent	19	none	No pyuria 6 mos.	none	good
A. D.	7/2/52	34	Permanent	14	8 dys.	No pyuria 26 dys.	none	good

readily accomplished by attention to anatomy and surgical technique Anatomically, the wall of a hydronephrotic sac is supplied by small arteries extending downward from the renal hilus, fanning out over the dilated pelvis and anastomosing distally with arteries extending up from the ureter Very few direct branches enter the pelvis itself and this fact is exaggerated by the pathological dilatation Thus, the center portion of the dilated pelvis can be removed without interrupting essential arteries The portions of pelvic tissue which are to be saved need not be separated from their respective connective tissue beds and blood supply Mobilization should be done only to the extent that it is absolutely necessary This is facilitated by doing most of the dissection from inside the pelvis after it is once open Damage to the tissue is minimized by using tissue hooks and fine forceps With proper respect for these factors one will find that the tissue ends continue to bleed until sutured together Healing is then prompt and fibrosis is minimized

Diversion of the urinary stream by nephrostomy is necessary to prevent post operative distention and extravasation It should be maintained 14 days or longer

Another valuable aid to proper healing is the ureteral splint, or intubation of the ureter Its usefulness has been well proven by the work of D M Davis, Weaver and others It not only tends to immobilize the area but maintains the lumen during the healing period The Cummings nephrostomy tube has been very satisfactory

RESULTS

Estimation of results is based on the following criteria 1) permanent relief of pain, 2) prompt closure of the nephrostomy, 3) rapid disappearance of signs of infection, 4) freedom from recurrent infection, 5) pyelographic evidence of improved drainage and funnel, 6) improved function (See table 1)

An unusual opportunity for visual evaluation of results was offered in case 8, a 6 year old boy A pyeloplasty was done on August 17, 1951 At the operation a 2 by 6 cm segment of renal pelvis was removed The postoperative course was uneventful, urine was free of infection 70 days after operation Seven months after surgery, the patient had an attack of gross hematuria, investigation of which revealed a small renal stone which had developed on the suture line On April 18, 1952, the left flank was reopened The perirenal and periureteral regions were found remarkably normal, with no thickening or induration, and only minimal adhesion The ureteropelvic juncture was smooth and conical It was with difficulty that the site of anastomosis was identified A longitudinal incision was made on the posterior wall of the pelvis, through which a 1 by 1 cm calculus was found attached to the anterior pelvic wall It was removed The ureteropelvic stoma readily admitted a 4 mm probe, and was soft, pliable, and freely movable On suturing the pelvis, no attempt was made to produce a watertight closure Following operation no urine drained from the flank, and the patient was discharged in 8 days with the wound closed and dry He has had no further trouble

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THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

THE CURRENT STATUS OF THE CHEMOTHERAPY OF RENAL TUBERCULOSIS

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During the last 9 years, since the advent of streptomycin, we have been looking for some evidence of a new decline in the incidence of renal tuberculosis. It has seemed reasonable that with better control of pulmonary tuberculosis, we might, at about this time, expect to see some decline in the incidence of the blood-borne complications, such as renal tuberculosis. With that in mind, we have made a survey of the case material of the last few years, to see if we could detect any such decline. A review of the number of new cases treated in each of the past 5 years by the Veterans Administration, Army and Navy Cooperative Study revealed no significant decline.

We then checked the other sources of our material and found that the numbers of new cases at the pilot study unit at the Bronx Veterans Hospital again showed no significant decline in numbers of patients diagnosed during the past 5 years. In the year 1955, we have even seen an increase in the numbers of new cases diagnosed. We then checked the new cases at the Presbyterian Hospital in New York City, and again found no evidence of a decline during the past 5 years.

It may occur to you that we might have a large number of referred cases of renal tuberculosis at our hospital, because of our interest in this disease, and that they might distort our totals. However, all referred cases have been excluded from these figures on incidence. We have included only cases detected in local practice.

Only among children with tuberculosis (miliary and other) did we find a decline in the incidence of new patients with positive urine cultures for M. tuberculosis. On our pediatric urological service, we have seen no new cases of urinary tuberculosis in the years 1953, 1954, and 1955 whereas there were always a few previously. This decline has come since the adoption of "triple drug" therapy for miliary tuberculosis.

Over the past 8 years various chemotherapeutic regimens, using streptomycin alone, isoniazid alone, streptomycin plus PAS and the combination of streptomycin, PAS, and isoniazid, have been tested for effectiveness on groups of our patients with renal tuberculosis who were highly comparable in all respects. All patients were treated and followed on the same wards, by the same personnel, and under as closely similar conditions as possible during the 8 year period. It was recognized that these groups were not run as concurrent controls against one another, but they were run in serial fashion with the minimal possible interval between groups. These conditions were made necessary by the

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Read at annual meeting, American Association of Genito Urinary Surgeons, Pebble Beach, Calif., May 23-25, 1955.

small numbers of patients available and by the discovery of new drugs as time progressed.

The severity of the renal lesions treated was highly comparable in each group of patients. All had renal lesions of moderately or far advanced cavitary type. Patients with minimal renal lesions (with no pyelographic cavities) were not included in these studies due to the fact that such lesions are so easy to arrest that they do not constitute a good test of the treatment. It was believed that the advanced lesions provided a much more rigorous test of the effectiveness of each regimen. It was also kept in mind that most of the renal lesions which are seen by the urologist are advanced lesions when first observed.

RESULTS OF TRIPLE DRUG THERAPY

The most effective drug regimen tested to date has been the combination of streptomycin 1 gm. twice weekly, isoniazid 100 mg. t.i.d. and sodium PAS 5 gm. t.i.d., all given simultaneously for one continuous year. Figure 1 shows a comparison of the results of treatment with three different chemotherapeutic regimens to date. It should be noted that the group of patients who received the triple drug regimen has shown no relapses of the urine cultures to positive, since the initiation of treatment. A group of 20 of these patients has completed 1 year of treatment plus 1 year of followup, at this writing. The fact that more relapse

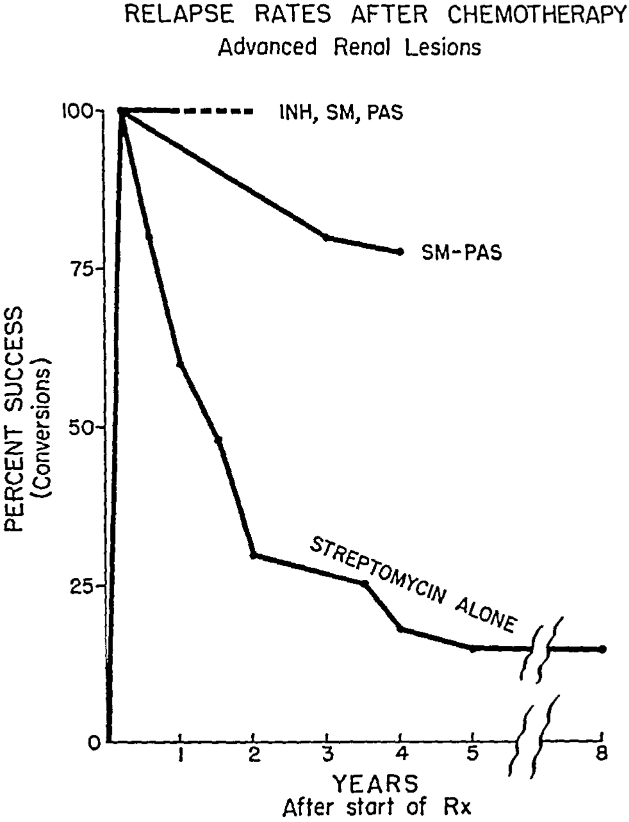

FIG. 1.

have not occurred by this time appears to indicate an advantage for the three drug regimen (isoniazid, streptomycin, PAS) over the two drug regimen (streptomycin, PAS) It is to be expected that some relapses will occur in the future, but none are apparent at this time

Bed rest, of a semi-ambulatory type, is considered an important adjunct during the first six to twelve months of this treatment It is also important that the patients take full doses of the medications and skip no doses It is our practice to give these patients therapeutic vitamin therapy throughout their treatment This regimen has been so successful to date that we have not removed any tuberculous kidneys or portions of kidneys at the Research Unit for Genito Urinary Tuberculosis in the past 3 years One kidney was removed for study (see below) Should relapses occur, we will precede any surgical procedures with one month of isoniazid plus sodium PAS and follow the operation with eleven months of isoniazid and sodium PAS

HISTOLOGY OF RESECTED LESIONS

One of our patients died of cardiac disease immediately after the completion of 1 year of triple drug therapy At necropsy the right kidney was found to contain the expected scar at the position of his pyelographic lesion Ureteral urine cultures from this kidney had been positive for M tuberculosis prior to treatment His voided urine had been repeatedly positive for M tuberculosis before treatment The urine cultures from all of these sources had become negative during and after treatment On histological examination of the scar, the pathologist found no evidence of tuberculosis No acid fast bacilli could be grown from the kidney A similar disappearance of the histological characteristics of tuberculosis has since been reported from England by Dr Dick of the British Research Council Four out of 25 of the kidneys which he examined showed a disappearance of the tuberculous histology after chemotherapy

In another of our patients, who had received triple drug therapy for 1 year, the kidney was removed for pathological examination, upon completion of treatment Prolonged attempts were made to grow M tuberculosis from the massive caseous kidney lesions by Dr Gladys Hobby of the Pfizer Chemical Co, who has been so successful in culturing viable tubercle bacilli from resected lung lesions Growth was obtained by Dr Hobby, from these kidney lesions, only after 7 months of incubation The histological characteristics of the far advanced lesions in this kidney showed a tendency toward healing but not complete disappearance of the changes due to tuberculosis The pathological examination of this kidney was done by Dr Oscar Auerbach of the Veterans Administration Cooperative Study He suggested that further chemotherapy (18 to 24 months) might permit healing to become complete

Streptomycin 1 gm twice weekly, plus sodium PAS 5 gm t i d (two drug therapy) given together for 1 year proved much more effective than therapy with streptomycin or isoniazid alone, with only 20 per cent relapses after 4 years of followup It did not appear to matter whether the 1 gm of streptomycin was given daily or twice weekly, in combination with 5 gm sodium PAS daily

Giving streptomycin twice weekly was so much less toxic, and deferred drug resistance so well, that this dosage plan is now used. The factors that favored relapse in this group were: 1) less than one year of therapy; 2) older age of the patient; 3) coexisting pulmonary tuberculosis; 4) organisms already resistant to streptomycin due to prior treatment.

It was noted that prostatic tuberculosis responded to chemotherapy just as well as did renal tuberculosis.

CLORPACTIN FOR TUBERCULOUS BLADDER ULCERS

A new drug, "clorpactin 90," has been found effective in ameliorating the symptoms from tuberculous ulcers of the bladder. This is a topical medication which has a detergent action on the ulcers and also releases chlorine (as hypochlorous acid) in concentrations which are tuberculocidal. The symptoms from chronic tuberculous cystitis were markedly improved in most cases by the use of this medication as a bladder irrigation. These irrigations were moderately irritating, and had to be given several days apart.

INADEQUATE STERILIZATION OF CYSTOSCOPES

It was discovered that conventional methods used for "sterilizing" cystoscopes did not kill M. tuberculosis within one hour. Formalin vapor cabinets were unsafe (formalin vapor cabinets did not even kill B. proteus in 1 hour). Also solutions of mercuric oxycyanide, the quaternary ammonium compounds, and soaps were found unsafe for sterilizing cystoscopes which had been used on tuberculous patients. It therefore appeared conceivable that cross contamination between patients might occur if a cystoscope were used on a tuberculous patient and then used again on a clean patient within one hour. It was demonstrated, by our tests, that immersion in a 10 per cent formalin solution for a period of 5 minutes would kill M. tuberculosis on cystoscopes, provided that the cystoscopes had been washed with soapy water previously and that all stopcocks and lumina were open. It did not harm the cystoscopes. If formalin is objectionable, for any reason, the instrument germicide manufactured by the Lehn and Fink Co. has been found to be effective in killing M. tuberculosis if the cystoscopes are immersed in it for 1 hour. All of the solutions had to be washed from the cystoscopes so that they would not irritate the tissues of the patient. It was found that catheters and other instruments which could be boiled for 5 minutes were best sterilized by this method.

SUMMARY

Triple drug therapy (isoniazid, streptomycin and sodium PAS), given for 1 year, appeared to be more effective than double drug therapy (streptomycin plus PAS), in the treatment of renal and prostatic tuberculosis, and is our current treatment regimen. Bed rest, plus a high vitamin intake, were combined with the chemotherapy. Prolongation of the treatment to 18 or 24 months may be even more effective. To date, no new decline in the incidence of renal tuberculosis has been observed, despite the advent of chemotherapy.

Chlorpactin was found to be an effective new topical medication for tuberculous ulcers of the bladder

Immersion of clean cystoscopes in a 10 per cent formalin solution for 5 minutes proved to be an efficient and harmless method for sterilizing instruments contaminated with M tuberculosis

We wish to acknowledge our indebtedness to our bacteriologists, Dr Michael Kenney and Mr Goldman, to our head nurse Miss Lydia Sechler, to our secretaries Mrs Barbara Schindler and Mrs Anne Machino, and to the members of the Departments of Urology, Radiology, and Pathology of the Kingsbridge Veterans Administration Hospital who have co operated so well in this study

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

ANEURYSM OF THE RENAL ARTERY

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Although the occurrence of renal artery aneurysms is rare (1:8,000 autopsies), the prognosis of the untreated case is so extremely grave that the practicing urologist should acquaint himself with the entity. Excellent reviews of the reported cases have been written, the most recent being an exhaustive survey by Abeshouse in 1951. He redefined a *true aneurysm* as one with one or more of the original coats of the artery; a *false aneurysm* as one whose wall originated from tissue outside the renal artery. He listed 80 true aneurysms and 35 false aneurysms for a total of 115 cases. Since then three more cases of true aneurysm have been reported bringing the total of true aneurysms to 83 and the overall total to 118 cases.

All authors have stressed the characteristic signet-ring or halo-shaped calcification just medial to the renal pelvis as pathonomonic. Unfortunately, only about 25 per cent of all cases display this calcification. This one-fourth of the cases should be diagnosed preoperatively. The other 75 per cent are discovered secondarily either during surgery for another cause, or at the time of rupture of the aneurysm.

The symptom complex from renal artery aneurysm is varied and unreliable. We were impressed in our experience by the hypertension, as it was this sign that led to diagnostic studies in both of our cases. The tabulated symptoms and signs with their percentage of occurrence are:

Pain	50 per cent
Hematuria	35 per cent
Mass	25 per cent
Hypertension	15 per cent
Bruit	10 per cent

At least four cases in a series of 12 with preoperative hypertension returned to normotensive levels following nephrectomy.

It seems agreed that immediate surgical excision of the aneurysm is the treatment of choice. Usually this means nephrectomy, but several cases of conservative surgical excision have been carried out where the aneurysm was in a small branch of the renal artery. The nonsurgical management of these aneurysms has been uniformly fatal from eventual rupture.

In 1929 Carson reported a case of a 62-year-old man found to have bilateral renal aneurysms post mortem. We would like to present another case of bilateral renal aneurysms diagnosed by x-ray 2 years prior to death (case 1).

CASE REPORTS

Case 1. Mrs. H. G. (U. H. 559639), a 25-year-old white woman, was admitted to the neurosurgical service of our hospital in December 1944, with severe

Accepted for publication July 20, 1955.

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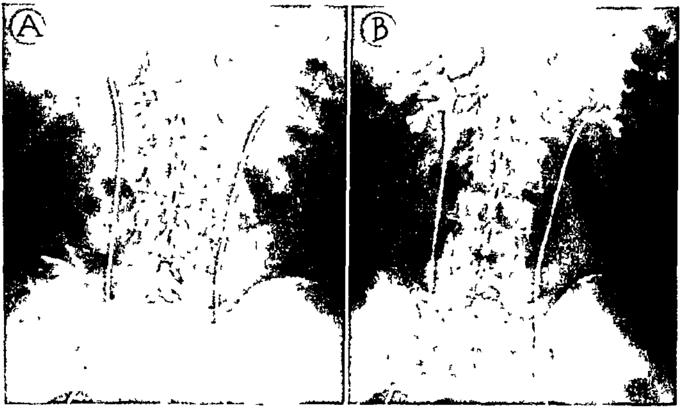

FIG. 1. Case 1. Twenty-five-year-old woman with severe hypertension. *A*, x-ray reveals bilateral renal artery calcification believed to represent bilateral renal artery aneurysms. *B*, pyelograms showing relationship of calcification to renal pelvis.

hypertension (blood pressure 256/158) with resultant occipital headaches and a right central scotoma secondary to a retinal hemorrhage.

Pre-splanchnicectomy workup revealed normal renal function tests and negative urine except for a trace of albumin. The patient gave no history of hematuria and physical examination of the abdomen was normal.

The pyelograms, however, were most interesting. The renal collecting systems were normal, but there were bilateral calcified opacities medial to the renal pelves and overlying the renal vessels (fig. 1). On the right the calcification measured 1 by 2½ cm. and had the appearance of a hollow calcium crust with two circular markings, one at either end. On the left a signet-ring shadow classical of aneurysm could be seen. Stereoscopic and oblique views placed these opacities in the renal vessels. A diagnosis of bilateral renal artery aneurysms was made. Split function phenolsulfonphthalein tests were essentially normal.

Bilateral thoracolumbar splanchnicectomy was carried out several weeks later in the hope of some palliative relief of this woman's symptoms, even though her hypertension was believed to be on a renal basis. She did gain relief from her headaches and the blood pressure dropped to 190/160.

In the fall of 1946 this patient became pregnant and by December of that year her hypertension rose to 240/120. She entered this hospital again for medical induction of labor (seventh month of pregnancy) only to suffer a cerebrovascular accident and succumb on December 21. Renal function tests were reduced to one half or less of their normal values.

Unfortunately postmortem examination was denied.

If a case of bilateral renal artery aneurysms occurs at the present time, perhaps the feasibility of replacement of the aneurysms with either plastic or homologous vessel grafts should be considered. It would be interesting to note the effect of such a graft on the patient's hypertension.

Case 2. Mrs. D. K. (U. H. 228975) is a 52-year-old white woman with a history of right costovertebral and right upper quadrant transient pains since 1935.

She was studied extensively in this hospital in 1939, when her difficulties were labeled as "probable chronic cholecystitis" with moderate psychogenic overlay. Studies at that time included complete gastrointestinal series, cholecystogram, retrograde pyelograms, and a chest x-ray. All these were normal. It is interesting to note that on the pyelograms the roentgenologist described a "rounded density just above the tip of the right ureteral catheter and probably outside the kidney". In retrospect this density must have been beginning calcification in a renal aneurysm.

In early 1953 the patient underwent a cholecystectomy elsewhere, without relief of her right flank pain.

She again returned to this hospital's out-patient department several months

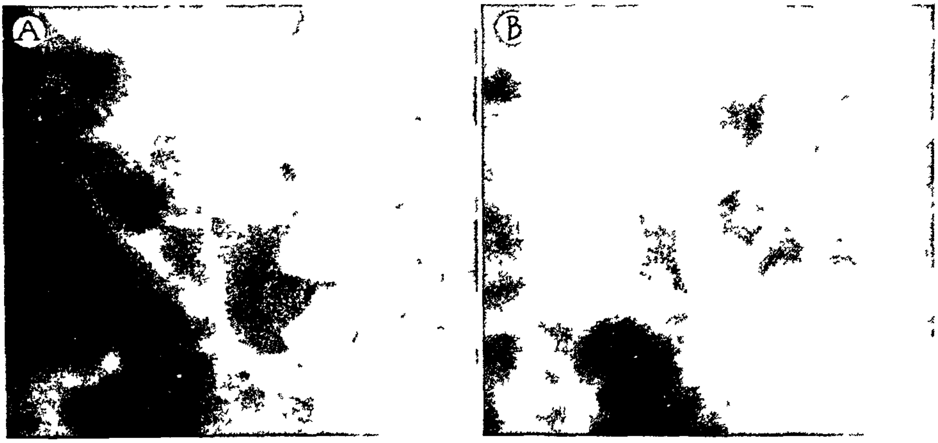

FIG. 2. Case 2. Signet-ring or halo calcification in hypertensive 52-year-old woman with persistent right upper abdominal pain. *A*, calcification is diagnostic of renal artery aneurysm *B*, pyelogram shows relationship of calcification to pelvis.

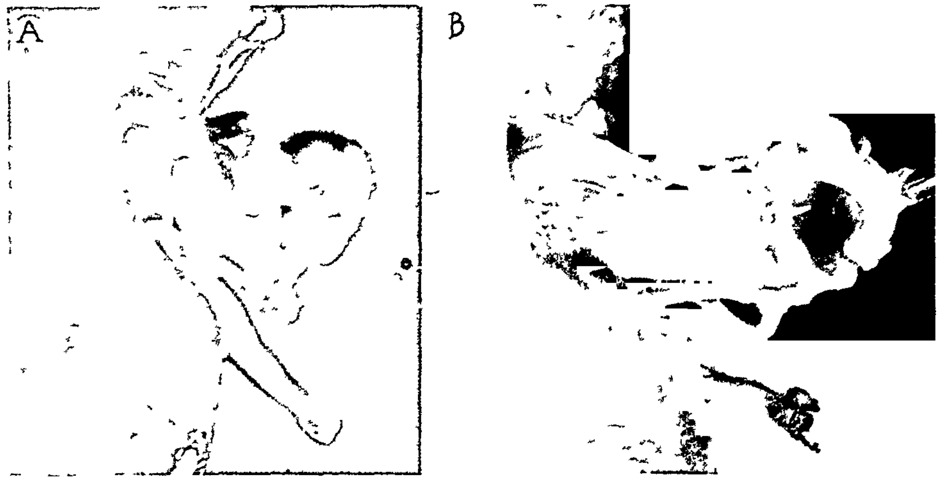

FIG 3. Case 2 (same case as figure 2). *A*, gross specimen prior to opening aneurysm. Note multiple renal artery tributaries distal to saccular aneurysm *B*, aneurysm has been opened Hemostat grips proximal renal artery.

later and was noted to be hypertensive (blood pressure 170/105) Her blood pressure had been normal in 1939

Excretory urograms during that visit revealed the characteristic signet-ring calcification just medial to the right renal pelvis with some compression of the pelvis itself (fig 2) The diagnosis of right renal artery aneurysm was entertained and the patient was asked to return to the hospital for further investigation She failed to return until 1955

In February 1955 the patient was admitted to this hospital Excretory urography again revealed the pathonomonic signet-ring calcification in the region of the right renal artery Aortography was not done as the diagnosis had already been ascertained, and the danger of rupture was a real one Right nephrectomy was carried out February 11 and a 2 cm saccular aneurysm of the main trunk of the renal artery removed (fig 3) The aneurysm was noted to arise from the bifurcation of the artery making conservative surgery impossible

Pathological report verified the diagnosis of true renal artery aneurysm with calcification The kidney itself showed no evidence of ischemia or atrophy

This patient had never noticed hematuria At the time of nephrectomy her urine was clear

Immediately postoperatively her blood pressure fell to 120–130 systolic over 70–80 diastolic Six weeks following surgery it rose to 150/70 She is now completely free of pain

In summary, 25 per cent of renal artery aneurysms can be diagnosed by their characteristic signet-ring calcifications They should be treated by nephrectomy to prevent 1) rupture and possibly 2) hypertension

These two reported cases constitute the a) 84th and 85th true renal artery aneurysms, b) 119th and 120th reported renal artery aneurysms c) second case of bilateral renal artery aneurysms

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* Arranged chronologically

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

PATHOLOGY OF TUMORS OF THE RENAL PELVIS AND URETER

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In considering the pathology of tumors of the renal pelvis and ureter, one immediately ponders the problem of etiology. Perusal of this line of thought leads one into the multiple ramifications of conflicting views and terminology. An endeavor to reassemble these thoughts in some order of sequence necessitates the acceptance of certain fundamental facts and concepts.

EMBRYOLOGY

A study of the embryological origin of the kidney, ureter and bladder sheds some light on the pathology of tumors in these organs. For the embryology, Arey has been consulted, and is quoted freely without endeavoring to credit exactly individual sentences or words.

In the human embryo, the kidney develops in 3 stages. The first stage is the *pronephros*, which is a provisional, but functionless kidney.

The second stage of development is the formation of the *mesonephros* or wolffian body which is called the "middle kidney" since it is located more caudally. The tubules from the mesonephros drain into the pronephric duct (which was retained), but now becomes known as the mesonephric or wolffian duct. The mesonephros acts as a temporary excretory organ.

The third stage of development is the formation of the *metanephros* or permanent kidney. As in the case of the mesonephros, the metanephros consists of an aggregate of tubules which drain into a common duct. Here, however, the secretory unit or nephron (including Bowman's capsule, proximal and distal convoluted tubule, and Henle's loop) is formed from the caudal end of the *nephrogenic cord* (i.e., has an origin similar to that of the entire mesonephric tubule). The inert portion of the drainage ducts (ureter, pelvis, calyces, papillary ducts and straight collecting tubules) is derived from a bed growing from the mesonephric duct. The secreting tubule and the collecting tubule then unite to form a continuous *uriniferous tubule*. In structure and function these two components remain as different as was their origin.

The mesonephric duct makes a sharp bend just before entering the cloaca. It is at this site that the *ureteric bud* develops. The proximal part of the bud elongates to form the future ureter and the distal part forms the *renal pelvis* which pushes its way into the metanephrogenic mass above (which is the caudalmost portion of the nephrogenic cord). This mass promptly separates, and surrounds the pelvis, to become the permanent kidney.

Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23-25, 1955.

The epithelium of the collecting tubules in the metanephros (which were derived from the nephrogenic cord) develops a tall columnar type of epithelium. The epithelium of the calyces, pelvis, and ureter (developed from the mesonephric duct), on the other hand, forms a stratified epithelium known as a *transitional epithelium.*

In vertebrates below the placental mammals, fecal, urinary, and reproductive products all pass into a common entodermal chamber. Higher mammals (man) have subdivided this cloaca into a dorsal rectum, and a ventral bladder, urethra and urogenital sinus. Two separate outlets were formed, one for urine and the other for fecal discharge.

When the bladder finally emerges as a separate entity, it still receives on each side the common stem of a mesonephric duct and ureter. Growth processes quickly lead to the absorption of the common stems, resulting in 4 ducts with separate openings. By further shifting, the mesonephric ducts open at an elevation on the future urethra (known as Muller's tubercle). The two ureters come to lie well apart from each other at the superior corners of the triangular area (trigone). Temporarily this triangular area is an island of mesodermal epithelium amid the general entodermal lining of the bladder. However, it is soon replaced by encroaching sinus epithelium, so that the trigone is finally entodermal also. The general organization of the bladder, with the formation of its stratified epithelial lining (transitional epithelium), is attained during the third month of fetal life. Thus, early in embryonic life, the bladder, ureter, and renal pelvis are lined with identical and continuous epithelium which is transitional in type. This explains why tumors arising in any of these three areas are similar in type and may be identical in histological appearance.

ETIOLOGY

The epithelium of the urinary bladder, ureter and renal pelvis is identical, and is called transitional in type. It varies from 1 to 6 cell layers in thickness. The superficial layers are constantly being cast off, to be replaced by newly formed cells from the deeper staining basal layer.

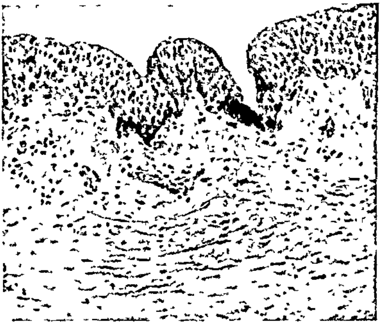


FIG. 1 Section of ureter showing normal transitional epithelium

A cross section of a ureter (fig. 1) consists from the inside out of:

1) Mucosa—a lining layer of transitional epithelium which may be from 1 to 6 layers deep. The basement membrane is not distinct, and blends intimately with the connective tissue of the tunica propria.

2) Tunica propria—composed of dense connective tissue intermingled with elastic fibers. Occasionally it contains lymph nodules.

3) Muscle coats—3 more or less distinct layers: inner, longitudinal, middle circular, and outer longitudinal.

4) Tunica adventitia—which is loose fibrous connective tissue continuous with the exterior of the kidney above and with the exterior of the bladder below.

The changes which may occur in the epithelium are described below.

THE EFFECT OF CHRONIC IRRITATIVE CHANGES ON THE EPITHELIUM

A) Proliferative

B) Metaplasia

Chronic irritation may cause a proliferative form of pyelitis and ureteritis or epithelial metaplasia.

A) *Proliferative.* If the irritant causes a proliferation of connective tissue in the tunica propria so as to form granular or polypoid projections into the pelvis or ureter, the condition is referred to as: 1) ureteritis granulosa or pyelitis granulosa, and 2) ureteritis polyposa or pyelitis polyposa.

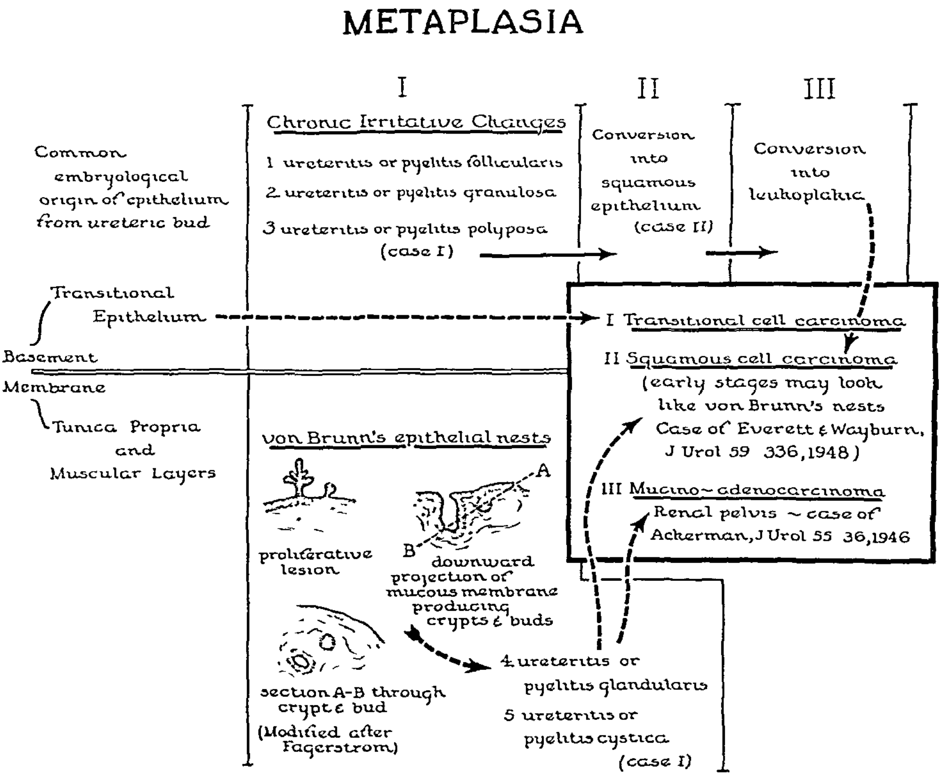

METAPLASIA
I
II
III
Chronic Irritative Changes
1 ureteritis or pyelitis follicularis
2 ureteritis or pyelitis granulosa
3 ureteritis or pyelitis polyposa (case I)
Conversion into squamous epithelium (case II)
Conversion into leukoplakia
Common embryological origin of epithelium from ureteric bud
Transitional Epithelium
Basement Membrane
Tunica Propria and Muscular Layers
I Transitional cell carcinoma
II Squamous cell carcinoma (early stages may look like von Brunn's nests Case of Everett & Wayburn, J Urol 59 336,1948)
III Mucino~adenocarcinoma
Renal pelvis ~ case of Ackerman, J Urol 55 36,1946
von Brunn's epithelial nests
A
B
proliferative lesion
downward projection of mucous membrane producing crypts & buds
section A-B through crypt & bud
(Modified after Fagerstrom)
4 ureteritis or pyelitis glandularis
5 ureteritis or pyelitis cystica (case I)

FIG. 2 Diagram showing changes of chronic irritation and metaplasia

When small lymph follicles are formed in the tunica propria, they also may elevate the epithelial lining, this change is called 3) ureteritis follicularis or pyelitis follicularis

If, however, the irritant causes a downward proliferation of epithelium into the tunica propria, there form solid nests of cells first described by von Brunn in 1893 These cell nests later develop a central cavity The condition is then referred to as 4) ureteritis cystica or pyelitis cystica Many of these cysts contain fluid which gives a positive reaction for mucin (case 1, fig 3) However, a lining

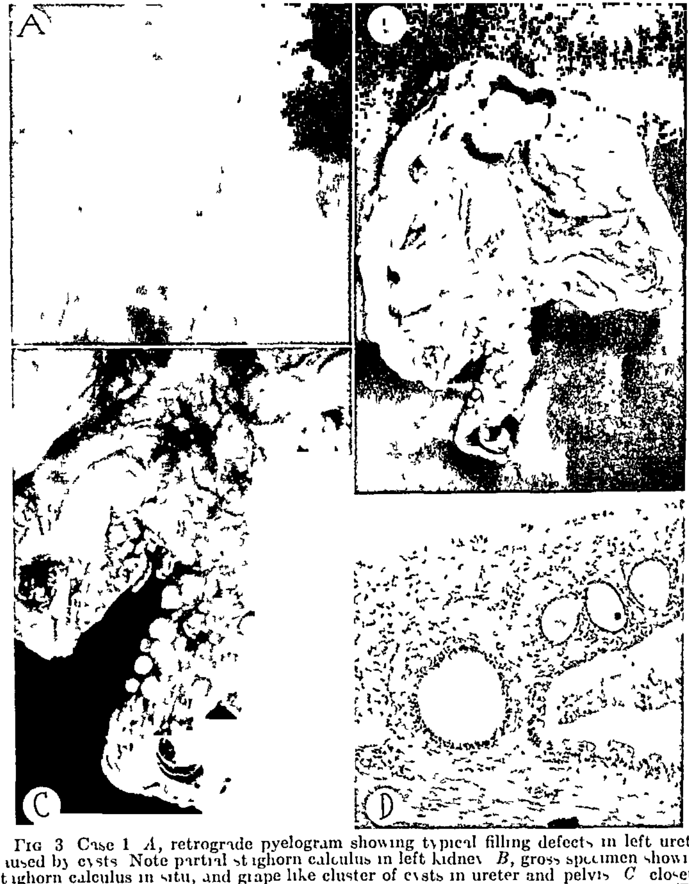


Fig 3 Case 1 *A*, retrograde pyelogram showing typical filling defects in left ureter caused by cysts Note partial staghorn calculus in left kidney *B*, gross specimen showing staghorn calculus in situ, and grape like cluster of cysts in ureter and pelvis *C* closeup view of gross specimen showing cysts *D* microscopic section of ureteritis cystica (Reprinted by courtesy of British Journal of Urology, MacLean Brit J Urol 26 136, 1954)

of typical goblet cells as occurs in mucinous metaplasia (or true pyelitis glandularis) is not present, and the overlying epithelium is transitional in type.

Stirling and Ash do not believe that the epithelial nests are the result of the downward proliferation of epithelium, but that they are the blind ends of mucosal crypts. They contend that if serial sections are properly cut through such an area, the alleged cell nest will always show a communication with the surface.

In Fagerstrom's detailed study of proliferation of tumors of the renal pelvis and ureter, it was not established that solid epithelial buds were the origin of solid tumors of the urinary tract. See figure 2.

B) *Metaplasia.* Epithelial metaplasia is the conversion of one type of epithelium to epithelium of another type.

1) Squamous metaplasia (changes to squamous cell epithelium): Prolonged irritation may lead to changes in the transitional epithelium which result in its conversion to a squamous cell epithelium characterized by thin platelike cells which are arranged in one or more layers that adhere to each other closely by their intercellular bridges. The cell layers eventually become more numerous with the formation of rete pegs and papillae. The squamous epithelium develops a line of keratinization, and there is desquamation of the surface cells into the lumen (case 2, fig. 4).

Leukoplakia by definition means "white plate." Keratin on the surface of squamous epithelium produces this white plate in the urinary tract. Although in some cases of squamous metaplasia, down growth and nuclear atypism may develop in the basal part, these changes are not necessary for the condition to be called leukoplakia. If atypical changes do develop, the lesion is only a step removed from malignancy.

2) Mucinous metaplasia: Here the lining is changed to a columnar epithelium containing goblet cells. With down growth of this epithelium, mucus secreting

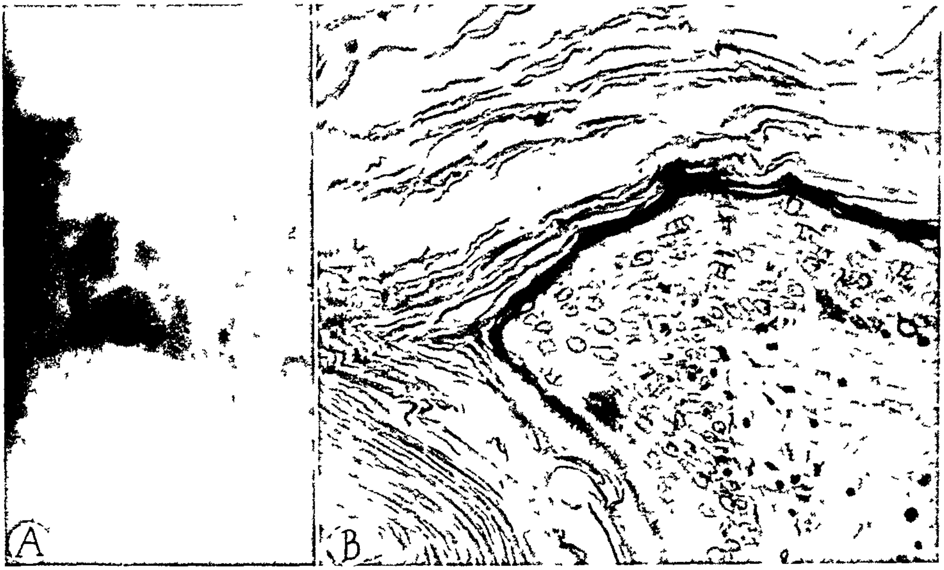


FIG. 4 Case 2 *A*, retrograde pyelogram showing filling defect in right renal pelvis. *B*, microscopic section showing squamous metaplasia of renal pelvis

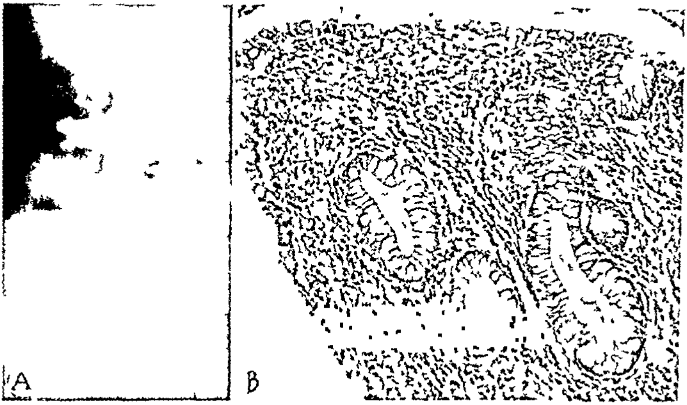


Fig 5 Case 3 A retrograde pyelogram showing staghorn calculus in right kidney and other calculi in lower pole B microscopic section showing mucinous metaplasia of renal pelvis Note columnar epithelium lining pelvis containing goblet cells and formation of mucinous glands which extend into tunica propria

glands are formed in the tunica propria They are lined by goblet cells and resemble enteric glands

However, metaplastic conversion of the transitional cell epithelium of the renal pelvis into the more specialized mucus producing epithelium of the type that occurs in the colon is an exceedingly rare phenomenon, and mucous adenocarcinoma of the renal pelvis correspondingly rare (Allen) Up to 1950 only two cases of mucous adenocarcinoma of the renal pelvis had been reported (Ackerman, Ragins and Rolnick) A third case of mucinous metaplasia of the pelvis and part of ureter was recorded by Plaut The authors wish to present a fourth case in which the renal pelvis only is involved In this case it is evident that the condition is a true mucinous metaplasia (case 3, fig 5)

The irritants which may produce the changes aforementioned are 1) long continued bacterial infection, 2) obstructive uropathies, 3) presence of calculus, 4) avitaminosis, especially of vitamin A, 5) hormone imbalance, 6) toxic products of metabolism, 7) specific carcinogens

Case 1 (fig 3) Renal calculus, left, pyelitis cystica, ureteritis cystica, cystitis cystica

N S, a man aged 44, was admitted to Queen Mary Veterans Hospital December 19, 1946, because a routine urine analysis showed albumin, red blood cells, and white blood cells He was entirely asymptomatic at this time

Physical examination Head and neck entirely normal Lungs normal Heart not enlarged, no thrills, no murmurs, no irregularities, blood pressure 170/110 Abdomen the liver was slightly palpable, but the spleen was not Neither kidney was palpable A left herniorrhaphy scar was noted Locomotor system entirely normal

Case 3 (fig. 5). Renal calculus; pyelitis glandularis—mucinous metaplasia of pelvis; hydronephrosis and chronic pyelonephritis minimal.

S. E., a woman aged 39, was first admitted to Royal Victoria Hospital December 5, 1947, at which time she had a lump in her right breast. This was excised, and the sections showed that it was a fibroadenoma.

She then remained well until July 1949 at which time she was admitted complaining of low back pain of 3 months' duration, and cloudy urine with a very heavy sedimentation. The remainder of the history was normal except that she stated she occasionally passed some blood in the stool.

Subsequent investigation revealed two calculi in the right kidney and one small opacity in the region of the left kidney. The opacity present in the region of the left kidney appeared to be outside the urinary tract.

A barium enema showed a deformity in the region of the rectum suggestive of a carcinoma of the rectum. This was confirmed by sigmoidoscopic examination when the diagnosis of an anterior lesion of the rectum was made and biopsy proved it positive. This was followed by a combined abdominoperineal resection of the rectum with a permanent colostomy. The pathological report showed that the terminal 26 cm. of the rectum and sigmoid had been removed, including the anus and surrounding skin. On the anterior wall of the rectum, 4 cm. above the anorectal junction, a polypoid, firm, dark-red, ulcerated tumor measured 2.5 cm. in diameter and 1.5 cm. in height. Sections of the tumor showed it to be an adenocarcinoma of the rectum limited to the wall of the rectum. Recovery was uneventful and the patient was discharged from the hospital 18 days postoperatively. In August 1952 she was readmitted to the hospital on the urological service, at which time a staghorn calculus was found in the right kidney. A nephrectomy on the right side was advised, but refused.

She was readmitted to the urological service on March 28, 1955, because of recurrent attacks of cystitis, burning, frequency of micturition, and urgency.

On admission, physical examination: Head and neck were normal. Thorax symmetrical, movements equal and bilateral; lungs: normal percussion note throughout both lungs, breath sounds normal, no rales or crepitations heard. Heart: not enlarged, no thrills; there was a slight blowing murmur in the mitral area heard in late diastole. The blood pressure was 180/110. Abdomen: there was no tenderness in either costovertebral angle; neither kidney was palpable; the abdomen showed the colostomy stoma functioning well; the surrounding skin was well healed. No abnormal masses were palpated.

The pelvic examination revealed a normal uterus in normal position and a normal appearing cervix.

Special examinations: Urinalysis: acid, specific gravity 1.020, albumin 3 plus; microscopic: 40 pus cells per high powered field; occasional red blood cell and bacteria.

An electrocardiogram was essentially normal.

Hemogram: hemoglobin 90 per cent; red blood cells 4,500,000; white blood cells 8,300. There was no gross abnormal finding in the hemogram.

Blood Kahn negative Blood nonprotein nitrogen 18 3 mg per cent

On April 1, 1955, a right nephrectomy was done

Pathology report The right kidney weighed 171 gm The thin capsule stripped with some difficulty to reveal a pale external surface with scattered irregular, depressed scars On section, the pelvis and calyces showed some dilatation and the distinction between cortex and medulla was lost in the scarred areas The pelvis and calyces were thickened and their surfaces were granular A few elevations measuring up to 3 mm in diameter were noted The 5 cm of attached ureter had a similar appearance

Sections of pelvis showed edema and a heavy infiltrate of lymphocytes and plasma cells in the tunica propria Epithelial erosions were noted in multiple areas In many areas the transitional epithelium was replaced by a layer of columnar epithelial cells, some of which contained droplets of mucus In the tunica propria deep to this metaplastic epithelium were numerous mucus secreting glands of the large bowel type There was no evidence of malignancy The kidney showed a few small focal areas of chronic pyelonephritis There was a mild exudative inflammatory reaction of the tunica propria of the ureter but no metaplasia Diagnosis Renal calculus, pyelitis glandularis—mucinous metaplasia of pelvis, hydronephrosis and chronic pyelonephritis—minimal

THE SIGNIFICANCE OF "PREDISPOSING FACTORS" AND OF SEEDING

The next important step is to recognize, as suggested by Ewing and by Waugh, that whatever the factors are that predispose to tumor formation in the urinary tract, there is no reason to believe that these factors are limited solely to the area in which the tumor occurs, but rather that the whole urinary epithelium is exposed to them This may explain the presence of multiple papillary tumors in the renal pelvis and ureter An alternative explanation is that "seeding" has occurred along the course of the ureter, from the parent growth above Either view could be supported by the statement of Whitlock, et al, in which they state that of 33 cases of primary carcinoma of the ureter, there were 10 instances in which bladder tumors developed after removal of the primary carcinoma of the ureter

The possibility of implantation by surface extension and spread along lymphatic channels is apparent

The theory of the spread of tumor from the bladder into the ureter by reflux regurgitation up the ureter is singularly lacking in appeal

THE CHEMICAL CARCINOGENS AND STEROIDS IN RELATION TO THE PRODUCTION OF CANCER

We are all familiar with the formation of bladder tumors in aniline dye workers, and of tumors of the scrotum in chimney sweepers It is interesting to note that in 1775, Percival Pott, the distinguished British surgeon, was the first to suggest the idea of cancer being an occupational disease, due to a specific material, a constituent of tar

This fact, and the subsequent progress of cancer research with its possible implications, are well described by Rhoads. In 1933 the British school of chemists led by Kennaway and his associates Cook, Dodds and Heiger succeeded in isolating from tar, the cancer producing substance which was named 1:2 benzyprene. The molecular configuration was established. Other compounds of a similar type were prepared synthetically.

Shortly after this, "the molecular composition of pure male and female hormones was described. It was obvious that the cancer-producing substance from tar and the steroid sex hormones had some similarity." "The chemical relationship between carcinogen and steroid hormone suggested, of course, the most important concept since the observation of Pott. This was that cancer in man may be due perhaps to a manufacturing mistake by the body in which there is formed a carcinogen instead of a natural hormone."

Scott and Boyd in 1953 added another brilliant chapter to our knowledge on the relationship between carcinogenic agents and the production of cancer. They were the first to produce experimentally early proliferative neoplastic lesions of the ureter and kidney pelvis, and primary carcinoma of the ureter using a known carcinogenic agent. They produced early proliferative neoplastic lesions after 32 months of beta-naphthylamine administration in a dog where stasis followed a right ureterosigmoidostomy. Carcinoma of the ureter was produced after 31 months' administration of the drug in animals where stasis had followed this implantation of the ureter into the isolated sigmoid bladder. They concluded that in addition to an unknown or known carcinogenic agent, urinary stasis might well be a contributing factor in the production of neoplastic lesions.

We have all pondered for some years the relationship between the excretion of steroids in the urine and the production of cancer. Cases have been reported in which bladder tumor apparently disappeared after the ureters were transplanted to the bowel.

INCIDENCE: AGE: DISTRIBUTION

Scott in his excellent chapter on tumors of the ureter in Campbell's *Urology* draws attention to the increasing frequency of reports on primary carcinoma of the ureter. Whitlock, et al., in reporting on 33 cases, state that there are now 312 reported cases of primary carcinoma of the ureter in the literature. Scott also notes that there have been 72 cases of primary benign tumors of the ureter recorded. The ratio of benign tumors of the ureter to malignant tumors is therefore approximately 1:4 (or 25 per cent benign).

From the years 1925 to 1954 inclusive, there have been 4 cases of primary carcinoma of the ureter operated on at the Royal Victoria Hospital. Of these 4 tumors, three were papillary infiltrating transitional cell carcinoma grade 2, one was papillary noninfiltrating transitional cell carcinoma grade 1. During the period 1932 to 1954 inclusive, there has been 1 case of primary carcinoma of the ureter found in 10,223 successive autopsies. In the period 1946 to 1954 inclusive, there have been 6 cases of primary carcinoma of the ureter operated on in the Veterans' Hospitals throughout Canada, and one case found at autopsy.

Age. In the benign tumors, the youngest reported is in a boy of 10, and the oldest is in a patient age 78. In the malignant tumors, the youngest reported is age 22 in a female, and the oldest in a man of 89. The commonest age group for all types of tumors of the ureter, both benign and malignant, is that between 40 and 80 with approximately 60 per cent in the fifth and sixth decades of life.

Sex. Malignant tumors of the ureter may occur in either the male or the female with a slight preponderance of the reported cases in the male.

Location of growth. Approximately two-thirds of all the tumors of the ureter occur in the lower third. The remaining one-third of tumors are approximately evenly divided between the upper and middle thirds of the ureter.

TUMORS OF RENAL PELVIS

MacKenzie and Ratner, reporting on a case of tumor of the renal pelvis, stated that at the Royal Victoria Hospital from 1917 to 1931 inclusive, there were 96 cases of tumor of the kidney, only one which was a true growth of the renal pelvis. Since then, from the years 1932 to 1954, inclusive, there have been an additional 111 kidney tumors operated on at the Royal Victoria Hospital. Of these, 14 had primary carcinoma of the renal pelvis: 5 were papillary noninfiltrating grade 1; 1 was papillary noninfiltrating carcinoma grade 2; 5 were papillary infiltrating carcinoma grade 2; 1 was papillary infiltrating carcinoma grade 3; (6 noninfiltrating, and 6 infiltrating transitional cell carcinomas) and 2 were infiltrating squamous cell carcinoma.

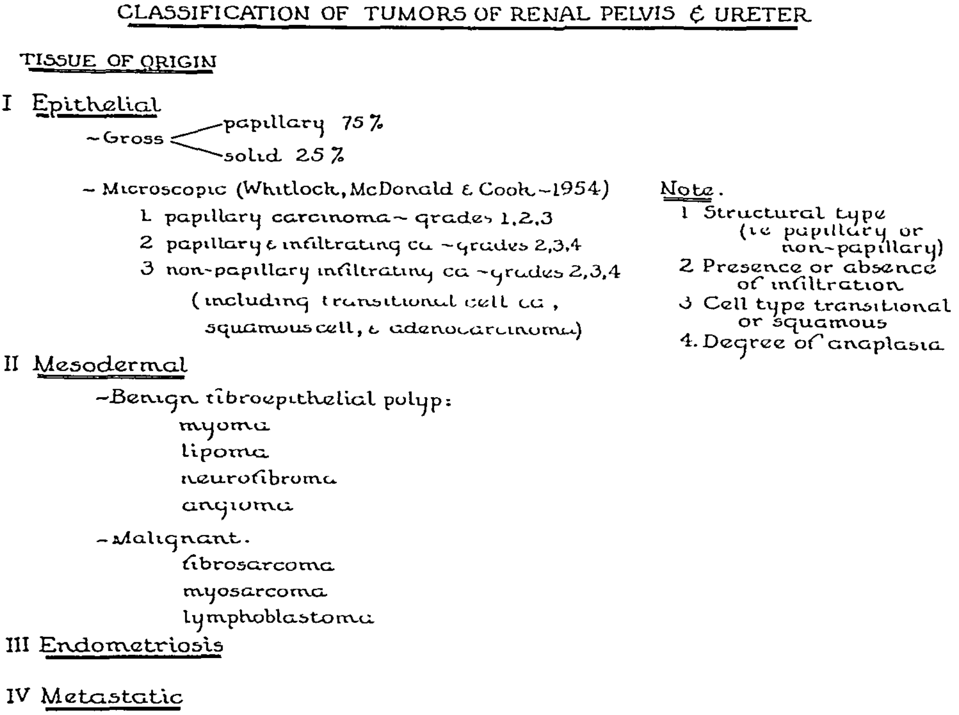
In the Veterans Hospitals in Canada from 1946 to 1954 inclusive there have been 164 cases of primary kidney tumor either operated on, or found at autopsy. Of these 18 were carcinomas of the renal pelvis.

Thus in the total series of 471 cases of primary renal tumor, 33 were carcinomas of the renal pelvis giving an incidence of 7.0 per cent.

Multiplicity of tumors. Thomas and Regnier in 1924 in a review of the literature on tumors of the renal pelvis found an incidence of 23 per cent with multiple neoplasms in the ureter or bladder, or both, associated with tumor of the renal pelvis. Stricker in 1926 found that in 47 per cent of 175 cases of papillomatous neoplasms of the renal pelvis, neoplasm was also present in the ureter and the urinary bladder. Whitlock, McDonald and Cook, in reporting on 33 cases of primary carcinoma of the ureter, have made the significant observation that in 10 instances, carcinoma of the bladder developed after surgical removal of a primary carcinoma of the ureter and, in some cases, years afterwards.

Classification of tumors of the renal pelvis and ureter (fig. 6). The primary tumors of the renal pelvis and ureter may have an epithelial or mesenchymal origin. Tumors arising from epithelium are of the transitional cell type, squamous cell type, or adenocarcinoma.

The cells forming the transitional cell tumors resemble, more or less, the epithelial cells of the normal mucosa. These tumors are divided into three types: papillary noninfiltrating, papillary infiltrating, or nonpapillary infiltrating. The cells vary from well differentiated to anaplastic and markedly pleomorphic. There is frequently variation in a single tumor. The degree of differentiation is indicated by cell grading according to the method of Broders.



CLASSIFICATION OF TUMORS OF RENAL PELVIS & URETER

TISSUE OF ORIGIN

I Epithelial
- Gross
  - papillary 75%
  - solid 25%
- Microscopic (Whitlock, McDonald & Cook – 1954)
  1. papillary carcinoma – grades 1, 2, 3
  2. papillary & infiltrating ca – grades 2, 3, 4
  3. non-papillary infiltrating ca – grades 2, 3, 4 (including transitional cell ca, squamous cell, & adenocarcinoma)

II Mesodermal
- Benign fibroepithelial polyp:
  - myoma
  - lipoma
  - neurofibroma
  - angioma
- Malignant.
  - fibrosarcoma
  - myosarcoma
  - lymphoblastoma

III Endometriosis

IV Metastatic

Note.
1. Structural type (ie papillary or non-papillary)
2. Presence or absence of infiltration
3. Cell type transitional or squamous
4. Degree of anaplasia

FIG. 6. Diagram showing classification of tumors of renal pelvis and ureter

As Willis states, "Although it is customary, and for clinical purposes useful, to distinguish between benign papillomas and carcinomas of the urinary tract epithelium, it is impossible to make any real pathological distinction between them."

In the above classification of Whitlock, McDonald and Cook, so-called papillomas are listed as papillary noninfiltrating carcinoma grade 1. There are no infiltrating carcinomas with a cell grade of 1, and all grade 4 tumors are of the infiltrating type. The presence or absence of infiltration, and the degree of infiltration are of greater prognostic significance than the cell grade.

Typical invasive squamous cell carcinoma may occur in the pelvis or ureter and occasionally there may be islands of squamous cell carcinoma in the invading portion of a transitional cell carcinoma. The squamous cell carcinomas are histologically similar to those of the skin and are recognized by the presence of intercellular bridges and keratin or pearl formation.

Mucoid adenocarcinoma is extremely rare.

Although the mesenchymal tumors of the renal pelvis and ureter are rare, it is theoretically possible to have tumors arise from any of the tissues which form these structures. The majority of the fibromas are polypoidal tumors with a covering of transitional epithelium. Other tumors include myomas, fibromyomas, neurofibromas and hemangiomas. Of the malignant mesenchymal tumors, leiomyosarcoma, and lymphoblastomas, including Hodgkin's disease, have been described.

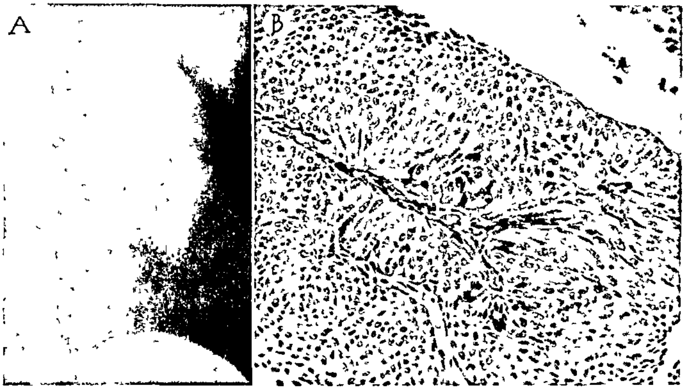


FIG. 7. Case 4. *A*, retrograde pyelogram showing deformity of left renal pelvis. *B*, microscopic section showing typical papillary transitional cell carcinoma in renal pelvis. Note thin central fibrous core, and mitotic figures.

Case 4 (fig. 7). Papillary infiltrating transitional cell carcinoma—grade 2—renal pelvis.

P. L., a man aged 61, was admitted to Ste. Anne's Military Hospital, March 2, 1945 complaining of intermittent hematuria over a period of 2 years, frequency and nocturia, day 8 to 10 times, night 4 to 5 times—of 3 days' duration; and suprapubic pain of 3 days' duration.

He gave a history of having had repeated attacks of gross hematuria while overseas during the past 2 years, but did not wish to report this to his medical officer for fear he would be sent home.

Physical examination: The patient weighed 267 pounds. His general appearance was excellent. The head and neck were normal. Lungs normal. Heart not enlarged; no thrills, no murmurs, no irregularities; blood pressure 140/85; abdomen: obese. There was slight tenderness in the left costovertebral angle. Neither kidney was palpated. The liver and spleen were not palpated. There were no abnormal masses palpated. The penis showed a first degree hypospadias, otherwise normal. Testes and epididymides normal. Rectal: sphincter tone normal. The prostate was enlarged about one and one half times normal size. It was fibroelastic, not fixed, not tender.

The urine was grossly bloody with scattered white blood cells in it. Nonprotein nitrogen 34 mg. per cent. Blood count: hemoglobin 95 per cent. Red blood cells 4,800,000. White blood cells 8,130. Phenolsulfonphthalein excretion test, done after the gross hematuria ceased, showed a 2-hour excretion of 40 per cent.

Excretory urography showed a normal sized kidney on the right side with some enlargement of the kidney on the left side. The right pyelogram was entirely normal in appearance. The left pyelogram was irregular in contour without any definition of the calyceal pattern in the upper pole and middle of the kidney.

Retrograde pyelography showed a normal pyelogram on the right and marked irregularity of the renal pelvis on the left with collections of dye in the upper pole and middle calyces of the kidney. This appearance was strongly suggestive of an intrapelvic tumor. Catheterized specimen from the right side showed a rare red blood cell and a rare white blood cell; on the left side there were 12 to 15 white blood cells and 1 to 2 red blood cells.

Twenty-four hour urine was examined for tuberculosis by smear, culture, and guinea pig inoculation. All reports were negative.

A diagnosis of tumor of the left renal pelvis was made. On March 19, 1945 a nephrectomy was done on the left side. Difficulty was encountered with the renal pedicle, as one vessel slipped out of the clamp. This was recovered, the bleeding was controlled. However, it was deemed inadvisable to carry out a dissection of the ureter at this time. The incision was therefore closed. Recovery was uneventful.

Pathological report: The left kidney weighed 280 gm. A large tumor with a rough, cauliflower-like surface filled the lower half of the pelvis and compressed and narrowed the parenchyma somewhat in this area.

Microscopic sections showed a papillary tumor with layers of cells covering thin connective tissue papillae. There was moderate cellular pleomorphism and occasional mitotic figures. There was superficial invasion of the wall of the pelvis. Diagnosis: Papillary infiltrating transitional cell carcinoma, grade 2; acute and chronic pyelonephritis.

Followup: The patient has remained well during the intervening 10 years. He was placed on a diet and reduced his weight to 195 pounds. His blood pressure remains at 140/85. Excretory urography done on January 24, 1955 showed normal function of the right kidney with an entirely normal pyelogram in which the major and minor calyces were clearly and delicately defined. The blood urea nitrogen is 22.9 mg. per cent.

Case 5 (fig. 8). Squamous cell carcinoma of renal pelvis.

J. B., a man aged 58, was admitted to the Royal Victoria Hospital January 10, 1944 complaining of gross blood in the urine, intermittently, for 1 year; pain in the right loin radiating to the back, for 1 month; frequency, nocturia and urgency, 2 weeks.

The past history was irrelevant to the problem concerned.

On physical examination, the eyes, ears, nose and throat were normal. The heart was not enlarged, there were no thrills, no murmurs, no irregularities. The blood pressure was 190/30. Lungs normal. Abdomen was obese; no tenderness and no masses were palpable. There was no costovertebral tenderness. Neither kidney could be palpated. On rectal examination the prostate was enlarged two to three times normal size. It was fibroelastic, not fixed, not tender and no nodules were palpated.

Laboratory investigation revealed that the specific gravity of the urine was 1.015; albumin 1 plus; sugar negative.

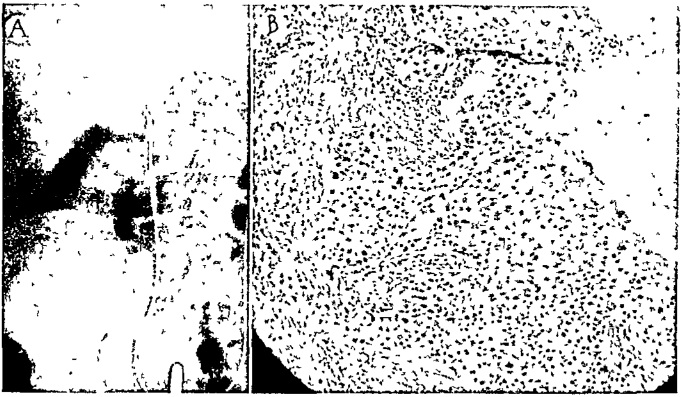


FIG. 8. Case 5. *A*, retrograde pyelogram showing filling defect in right kidney. *B*, microscopic section showing squamous cell carcinoma of renal pelvis.

The phenolsulfonphthalein excretion was 65 per cent in 2 hours.

Cystoscopy: With the patient under a low spinal anesthetic, the instrument was readily introduced. A large, black, ragged, oxalate stone, on the floor of the bladder, was found. Several growths were seen at the bladder neck, one in particular extending well into the right lobe of the prostate.

Under the same anesthetic, the bladder was opened, the stone removed, and a one-stage suprapubic prostatectomy performed. The prostate contained on its surface the tumor referred to at cystoscopic examination. The prostatic cavity was packed with an iodoform gauze and a Freyer tube inserted.

Pathological report: Sections of tissue from bladder neck showed a papillary tumor composed of delicate stalks of connective tissue covered by several layers of well differentiated epithelial cells. There were no mitotic figures or evidence of invasion. Diagnosis: Papillary transitional cell carcinoma grade 1 of urinary bladder.

Recovery was uneventful and the patient was discharged from the hospital 2 months after admission.

Progress report: Four months after the removal of the prostate and bladder tumor, cystoscopic examination failed to show any evidence of recurrence of bladder tumor. However, 2 months later, the patient was admitted to the hospital in an acute septic condition, complaining of pain in the right kidney region, intermittently, since his previous operation, plus an acute rise in body temperature of 1 week's duration with an increase of the pain in the right costovertebral angle.

Urine showed: albumin 1 plus, pus 4 plus; phenolsulfonphthalein excretion 40 per cent in 2 hours.

Cystoscopy showed a normal looking bladder with a white healed scar at the neck. Catheters were passed up each ureter, there was a good flow from the left, but a poor flow from the right. The pyelogram on the left side was normal and the pyelogram on the right side was deformed, the lower calyces failing to fill, and the upper ureter being slightly dilated.

A diagnosis of tumor of the right kidney plus pyonephrosis was made and a nephrectomy was carried out on August 10, 1944.

The patient ran a very stormy postoperative course and finally died 3 weeks after operation.

Pathological report: The right kidney weighed 490 gm. The capsule was thickened and stripped with difficulty from a finely granular surface. Cut section showed the cortical and medullary markings to be somewhat obscured. The pelvis was all but obliterated by firm white tumor which extended from this region into the renal parenchyma and through the capsule at one point. Approximately one-third of the kidney was replaced by a tumor mass with an irregular margin.

Sections showed a squamous cell carcinoma arising in the pelvis and invading the medulla and cortex of the kidney. Keratinization was prominent in some areas. Diagnosis: Squamous cell carcinoma of renal pelvis.

Case 6 (fig. 9). Squamous cell carcinoma of renal pelvis containing glands and mucin-secreting cells.

M. C., a man aged 54, was admitted to Royal Victoria Hospital March 11, 1955, complaining of pain in the abdomen after meals for 1 year and also pain in the right hip for 1 year.

The patient was last perfectly well a year ago when he began to notice pain in the epigastrium spreading laterally, coming on approximately 1 hour after meals. It was described as a dull ache and was relieved partially by alkalies. Over the past 2 months his bowel movements had become harder and in smaller quantities than previously; this despite glycerine suppositories. On one occasion he passed a little blood following a particularly difficult movement. Fried foods, coffee and jam gave him an acid feeling in his mouth. He had lost 20 pounds over the past year. Barium enemas in September 1954 and February 1955 were normal. For approximately the same period of time he had had a steady dull ache in the sacral region, apparently brought on at work when he lifted a heavy box and slipped, thereby wrenching his back. There was no radiation and no change in the pain since the onset. He had pneumonia in 1903; a fractured arm in 1903; gasoline burns in 1947. The patient had had a productive cough for 15 years, worse in the past 6 months. The sputum was greenish in color, approximately ⅓ to ½ cup a day. He had no chest pain. No frequency, urgency, burning or pain on urination; no hematuria. No history of venereal disease. Family history was noncontributory.

Physical examination: The patient appeared to have lost weight recently. Head and neck were normal. Chest: slight kyphosis, anterior-posterior diameter increased; percussion note resonant throughout. Breath sounds normal throughout; no added sounds. There was a draining sinus from beneath the right scapula. Blood pressure 178/88, pulse 76, regular and moderately strong; left border of heart 4 inches from midline. No murmurs heard. Abdomen was symmetrical in

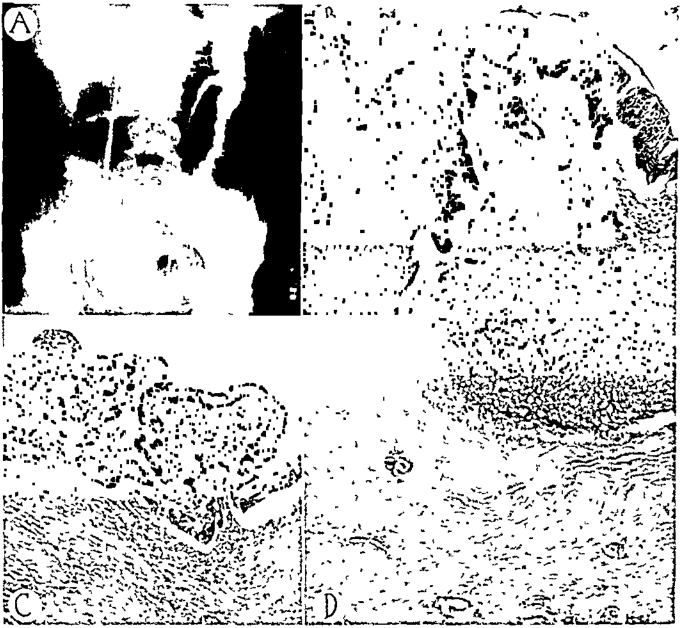


FIG. 9. Case 6. A, retrograde pyelogram showing obstruction at right ureteropelvic junction to the passage of dye. *B*, microscopic section showing invasive squamous cell carcinoma Note stratified squamous epithelium on surface. *C*, microscopic section showing invasive squamous cell carcinoma at another site (mucicarmine stain). A few droplets of mucin are present in overlying epithelium. *D*, microscopic section showing intra- and extracellular mucin (mucicarmine stain).

shape and movement; no enlarged organs, masses or tenderness; hernial sites clear. On rectal examination, sphincter tone good; no abnormal tenderness; no masses palpable; prostate not enlarged; a few hemorrhoidal tags externally. The right testis was firmer and slightly larger than left; otherwise negative.

Laboratory findings: Urine: *specific gravity* 1.020, *negative for albumin and* sugar, on 2 occasions a trace of albumin, sediments revealed 5 to 10 white blood cells and a few granular casts. Blood: hemoglobin 86 per cent; white blood cells 9,000, packed cell volume 44; sedimentation rate 30. Stool: negative for occult blood. Biochemical: A.C. sugar 75. Serology: Kahn negative. Glucose tolerance curve: slightly prolonged hyperglycemia. Gastric analysis: essentially normal.

Cholecystogram revealed, March 14, a gallbladder of normal outline which concentrated dye moderately well; no evidence of stone formation. A chest film revealed old empyema in the right chest with surgical drainage. A zone of increased density in this region probably represented fibrosis following this disease. There was no definite evidence of active parenchymal disease at this time.

Barium enema: normal. The esophagus functioned very well in the supine and upright positions. There was no evidence of esophageal varices. Lumbosacral spine: There was definite evidence of hypertrophic spondylosis. There was disc degeneration between T-12 and L-1 and probably between L-1 and L-2. No disease in the sacroiliac joint.

Progress note: The patient was transferred to general surgery on March 30, 1955 for abdominal exploration. This was performed on March 31 at which time a small, hard, fixed mass was located in the right renal area. Subsequent report of the biopsy showed the presence of cells in nests of the signet ring variety. Postoperatively, urological investigation was carried out. Retrograde pyelography showed the presence of a tumor of the right kidney; dye could not be introduced into the renal pelvis or calyces. The left pyelogram was normal. An aortogram was performed on April 16, 1955. The report in part was, "the right renal arteries are presumably obstructed since no dye has entered them."

On April 22, nephrectomy was performed. The kidney was found to be small, hard and fixed in position. By blunt dissection it was freed and removed. No bleeding was encountered from the pedicle; one small gelfoam pack was left in position.

The liver was seen to be greatly enlarged, but no nodules were palpable. Free fluid was present in the peritoneal cavity. Postoperative course uneventful to date.

Pathological report: Sections of perirenal tissue from the right side removed at laparotomy showed nests of epithelial cells in a connective tissue stroma. There were intercellular bridges in some of the nests and a few of the cells contained mucus.

The right kidney weighed 37 gm. It was firm in consistency and its thickened capsule was removed with difficulty from a pale grey, granular and pitted surface. The cut surface was grey in color and the interlobar and arcuate arteries presented as yellow streaks. Distinction between cortex and medulla was lost in multiple areas. The cortex measured up to 4 mm. in thickness. The calyces were slightly enlarged and irregular. They contained greyish gelatinous material. The epithelial surface of the calyces and the small pelvis was grey and granular. No plaques were present.

Four firm pieces of perirenal tissue, weighing 38 gm., were included with the kidney specimen. The cut surface of each piece was grey with irregular yellow-orange areas resembling adrenal cortex.

Multiple sections of kidney showed a marked fibrous replacement of cortex and medulla. The glomeruli for the most part were hyalinized and there was an infiltrate of lymphocytes in the interstitial tissue in those areas which were not replaced by dense scar. The large and medium sized arteries were almost completely obliterated by hyaline connective tissue. There was no amyloid in the kidney.

There was a carcinoma with multiple points of origin from the epithelial lining of the calyces. The tumor for the most part was squamous in type, with intercellular bridges and focal areas of keratinization. It infiltrated the small kidney diffusely and extended through the renal capsule into the perirenal tissues. Intracellular and extracellular mucus was present in many of the cell nests and there were a few gland-like spaces filled with mucus. Pseudo gland formation due to cell degeneration was prominent.

The lining of the calyces between the areas of invasive carcinoma varied from a single layer of flattened epithelial cells to epithelium of the stratified squamous type with intercellular bridges. Only a few droplets of mucus were present in the epithelium where it was transitional in type. Diagnosis: Squamous cell carcinoma with glands and cells containing mucus (mucoepidermoid carcinoma of renal pelvis).

Case 7 (fig. 10). Papillary, noninfiltrating carcinoma grade 2 of ureter; bronchogenic carcinoma.

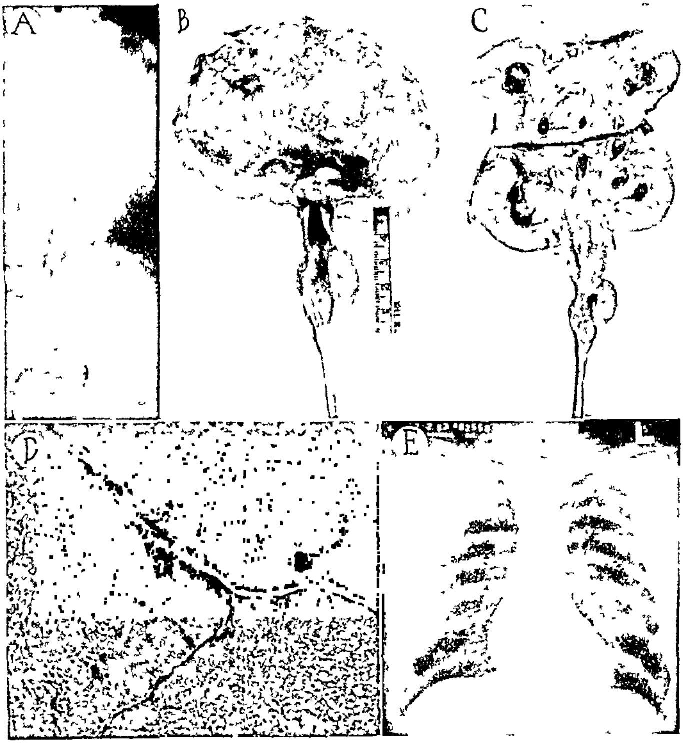


FIG. 10. Case 7. A, showing obstruction of dye near ureteropelvic junction on left side. B, gross specimen showing polypoid tumor in ureter. C, opened specimen showing hydronephrosis, and tumor in upper ureter. D, microscopic section showing thin branching connective tissue stalks covered by several layers of epithelial cells of a transitional type. Diagnosis: Papillary noninfiltrating carcinoma grade 2 of ureter. E, chest film showing lesion in right apex (bronchogenic carcinoma). (Reprinted by courtesy British Journal Urology, MacLean: Brit. J. Urol., 26: 236, 1954.)

S. B., aged 56, was admitted to Queen Mary Veterans Hospital on August 15, 1952 complaining of frequency and urgency.

The past history revealed that he had been under care of various D.V.A. hospitals since 1946. First admission was in October 1946 for chronic bronchitis and anxiety state. Second admission was in February 1947 for gross hematuria. He was found to have early middle lobe prostatic hypertrophy and prostatic calculi. No active treatment was instituted. The third admission was June 1, 1948 with the diagnosis of stricture of the urethra, mild hypertrophy of the prostate, and prostatic calculi. Dilatation of the urethra was carried out. There was no treatment given to the prostate. Excretory urography at this time showed no gross abnormality of either kidney. Kidney function appeared satisfactory. The fourth admission was in December 1949, as an outpatient, when he complained of his bronchitis, and "shakiness." The fifth admission to the Veterans Hospital was in March 1951, at which time a transurethral prostatic resection was carried out. The sixth admission was in July 1952 with the final diagnosis of phimosis, balanitis, left varicocele, chronic prostatitis, and chronic bronchitis. He was considered fit for work on discharge. One month later he was seen in the psychiatry section where a diagnosis was made of mental retardation and emotional instability.

Physical examination: Head and neck essentially normal. Thorax: Auscultation of the chest revealed sounds of fair quality in both lungs, with occasional rhonchi heard throughout both lung fields. The expansion was only fairly good on expiration. Heart normal. Blood pressure 155/100. Abdomen: There was a well healed appendectomy scar. Examination of the abdomen was otherwise normal; penis circumcised; testes normal; epididymides normal. Rectal: The prostate is slightly enlarged with increased fibrosis present. A previous diagnosis of prostatic calculi has been made.

Urine: Acid; specific gravity 1.025; albumin negative; sugar negative; microscopic: occasional pus cells seen and occasional epithelial cells.

Excretory urography showed nonfunction of the left kidney. At cystoscopy, the catheter was passed up the right ureter with ease to the renal pelvis. A catheter was passed up the left ureter as far as the transverse process of the third lumbar vertebra, where it met an obstruction. When dye was injected, the pyelogram on the right side was entirely normal. No dye passed beyond the point of obstruction at the third lumbar vertebra on the left side. The conclusion was that the patient had a nonfunctioning left kidney and that he probably had a nonopaque calculus on this side. It was decided therefore to explore the left kidney and ureteral region.

At operation on September 24, 1952, the point of obstruction in the ureter was felt and an incision made over it. Instead of a nonopaque calculus, a polypoid tumor of the ureter was found. A nephrectomy was done and included the upper 4 inches of ureter.

Pathological report: The pathological specimen showed a tumor mass in the ureter measuring 2 by 1.3 cm. It was attached to the wall of the ureter by a pedicle measuring 6 mm. in diameter, 2 cm. from the ureteropelvic junction. The pelvis was dilated.

Sections of tumor showed a poorly organized papillary growth. Several layers of epithelial cells of the transitional cell type covered a thin framework of connective tissue In many areas the papillary structure was lost and the tumor was composed of broad zones of epithelial cells separated by strands of vascular connective tissue There was a corresponding variation in nuclear atypism in different areas The wall of the ureter was not invaded Diagnosis Papillary noninfiltrating transitional cell carcinoma grade 2 of ureter, hydronephrosis and chronic pyelonephritis

Progress· On the postoperative re-examination of the patient, some 2 months after discharge from the hospital, the chest x-ray revealed an area of infiltration in the right upper lung field The patient was therefore readmitted to the hospital on February 11, 1953, when further investigation revealed that the infiltration in the right upper lung field was probably a bronchogenic carcinoma

On April 23, 1953, a right upper lobe lobectomy was performed, with section of the glands at the hylar region Microscopic sections of the tumor revealed it to be a bronchogenic carcinoma Recovery was uneventful and he was discharged from the hospital on May 12, 1953

Followup Five months later, on September 14, 1953, the patient was admitted to another D V A hospital where he died At autopsy, the following findings were noted. Bronchogenic carcinoma of right lung (lobectomy right upper lobe), secondary carcinoma of regional lymph nodes, right adrenal gland, large bowel and abdominal lymph nodes, organizing pneumonia, bilateral, acute bronchopneumonia, bilateral, acute splenitis, chronic prostatitis, atherosclerosis of aorta and coronary arteries (moderate)

Case 8 (fig 11) Papillary infiltrating transitional cell carcinoma grade 2 of ureter

J S, a man aged 70, was first admitted to the Royal Victoria Hospital in March 1948 at which time a two stage suprapubic prostatectomy was done

He was readmitted to the hospital on October 25, 1951 complaining of blood stained urine intermittently, of 10 months' duration The urine would become grossly bloody for 1 to 2 days at a time, and approximately at 10 day intervals Three months after the onset of the gross hematuria, the patient was investigated elsewhere and apparently told that there was decreased function of the left kidney No specific recommendations were given to him at that time

Physical examination Head and neck entirely normal Lungs normal Heart not enlarged, no thrills, no murmurs, no irregularities Blood pressure 120/68 Abdomen soft, well healed suprapubic scar No costovertebral tenderness No masses palpated Liver and spleen not palpated Neither kidney palpable Genitalia normal Rectal sphincter tone normal, the prostatic bed was fibrous and firm

Laboratory investigation Urine acid, specific gravity 1 008, albumin, a trace, sugar, negative, microscopic scattered red blood cells, rare white blood cells

Phenolsulfonphthalein test, 40 per cent in 2 hours

Electrocardiogram normal, chest film normal

Nonprotein nitrogen 23 mg per cent

Cystoscopy Bladder was normal Blood could be seen coming from the left ureteral orifice A catheter was introduced The catheter in the left ureter curled

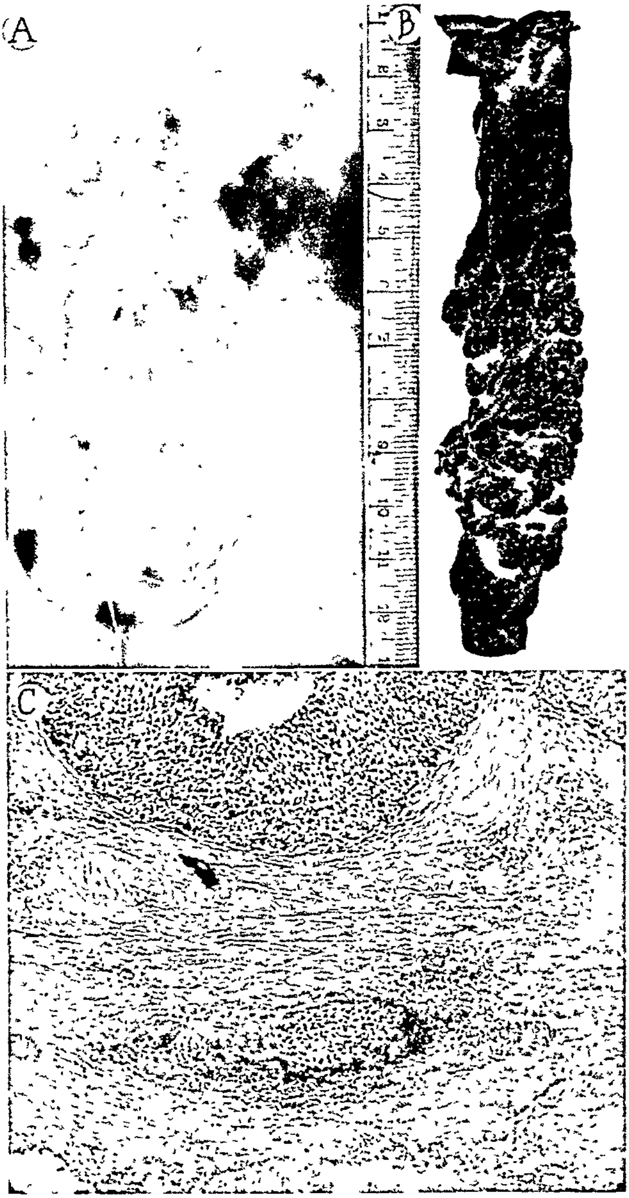


FIG. 11. Case S. *A*, showing catheter coiled in left lower ureter. *B*, photograph of gross specimen showing carcinoma in ureter. *C*, microscopic section showing transitional cell carcinoma grade 2 of ureter, invading muscularis. Tumor was papillary on surface. (Reprinted by courtesy British Journal of Urology; MacLean: Brit. J. Urol., **26:** 235, 1954.)

up in the lower ureter; the one in the right side was passed to the renal pelvis. When dye was injected, a normal pyelogram resulted on the right side, but on the left side the dye just returned into the bladder.

Excretory urography showed a normal right kidney and ureter with a nonfunctioning kidney on the left side.

A diagnosis of tumor of the left lower ureter was made and on November 3, complete left nephroureterectomy was done.

Pathological report: The left kidney weighed 115 gm. The external surface was rough, being both nodular and granular. The pelvis and calyces were markedly dilated and the renal parenchyma was narrow. The proximal half of the ureter was dilated up to 1.6 cm. in diameter. Tumor was present in 6 cm. of the distal half of the ureter. It completely encircled and extended into the lumen as a papillary mass. Two small nodules were present in the mucosa distal to this.

Microscopic sections of the tumor showed a papillary transitional cell carcinoma which invaded smooth muscle of the ureter in multiple areas. There was moderate cellular pleomorphism and a moderate number of mitotic figures. The nodules in the adjacent mucosa had a similar histological appearance. Diagnosis: Papillary infiltrating transitional cell carcinoma grade 2 of ureter; hydroureter, hydronephrosis, and chronic pyelonephritis.

Followup: Recovery was uneventful, and the patient was discharged from the hospital on November 24, 1951. He was readmitted 4 months later on April 2, 1952 at which time he had a recurrence of tumor in the bladder. A suprapubic cystotomy with excision of the tumor and coagulation of the base were done. He had four subsequent admissions from June 1952 to January 1954. On two occasions recurrence of tumor in the bladder was found, and treated by fulguration endoscopically.

On the last admission on June 23, 1954, a cystoscopic examination revealed no evidence of recurrence of the tumor in the bladder.

Case 9 (fig. 12). Papillary infiltrating transitional cell carcinoma grade 2 of ureter.

C. W., a woman aged 71, was admitted to the Royal Victoria Hospital on January 13, 1951, complaining of gross hematuria of 2 weeks' duration. During this time she passed a great many clots as well, and the hematuria had not decreased. Some dysuria was present during the first few days but had practically disappeared. She had mild frequency attributed to drinking large amounts of water in an attempt to clear up the bleeding. She gave no history of passing any sand or gravel, and no history of chills or fever. There was no loss of weight or strength.

Nine years previously, the patient had gross hematuria which caused her admission to another hospital. At this time a pelvic repair was carried out. Detailed investigation of the urinary tract was not done.

Physical examination: Breasts normal. Normal percussion note throughout both lungs; diminished breath sounds at both bases; no rales. Heart slightly enlarged. First sound was very loud, the second was practically inaudible. No thrills, no murmurs, no irregularities. Blood pressure 145/90. Abdomen soft. Striae gravidarum. No masses palpated. Liver and spleen not palpated. Neither kidney palpable. There was no costovertebral angle tenderness. Extremities normal.

Laboratory investigation: Urine: grossly bloody; albumin 2 plus; sugar negative; microscopic: loaded with red blood cells, occasional pus cells.

Blood nonprotein nitrogen 36.6 mg. per cent. Creatinine 1.27 mg. per cent. Kahn: negative.

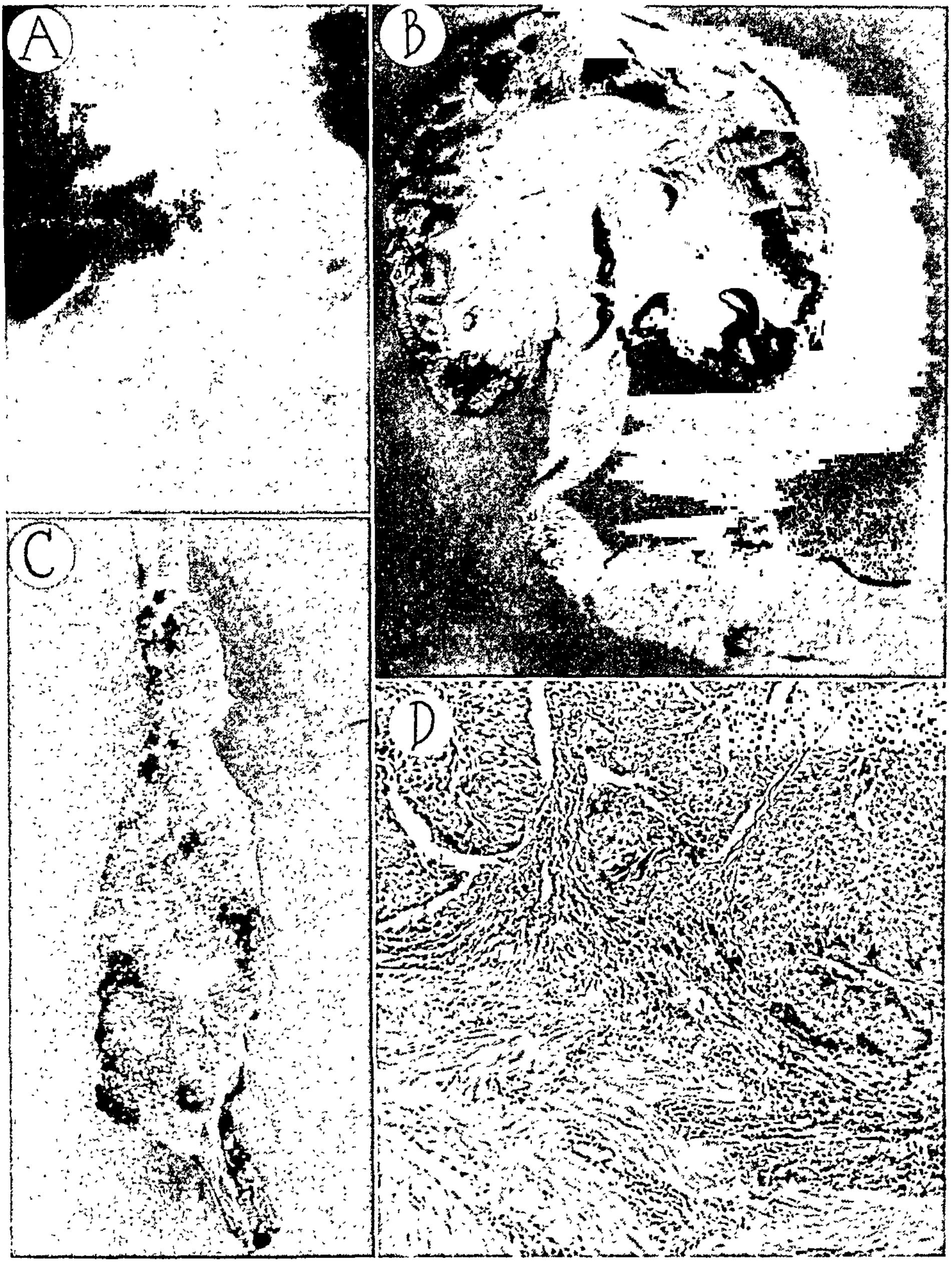


FIG. 12. Case 9. *A*, retrograde pyelogram showing hydroureter and hydronephrosis on right side. *B*, gross specimen showing kidney, and tumor in ureter. *C*, gross specimen showing closeup of tumor in ureter. *D*, microscopic section showing papillary transitional cell carcinoma grade 2, ureter. Note lymphocytic infiltrate at base.

Excretory urography revealed a normal sized kidney in normal position on each side. There were no opacities seen within the urinary tract. There was a calcified density in the region of the right bony pelvis which was probably the right ovary or a calcified fibroid. The left pyelogram was essentially normal. There was marked hydronephrosis and hydroureter on the right side.

Cystoscopy: The bladder was found to be inflamed and slightly ulcerated. The catheter was passed up the right ureter for 6 cm. at which point it met an obstruction. When dye was injected the ureter was seen to be very irregular.

A tentative diagnosis of tumor of the right ureter was made. A nephroureterectomy was advised, but refused.

The patient was discharged from the hospital and readmitted 1 month later (February 15, 1951) at which time a right nephroureterectomy was done. Recovery was uneventful.

Pathological report: The right kidney and attached 15 cm. of ureter weighed 135 gm. Only a few irregular, depressed areas were noted on the external surface. The cortex measured 4 mm. in thickness. The pelvis, calyces, and ureter were moderately dilated. The epithelial surface of the ureter commencing 6 cm. from the ureteropelvic junction and extending to within 1 cm. of the distal line of resection showed elevated granular and nodular, greyish, mottled red and brown areas which completely encircled the lumen. The wall of the ureter in this area was thickened and its pliability impaired. Its outer surface was smooth and glistening.

Sections of ureter through various portions of the tumor as well as uninvolved areas showed the usual transitional epithelium changing abruptly to tumor tissue. The tumor was papillary in nature and infiltrated the muscularis of the ureter in a few areas. The cells were of the transitional type and varied somewhat in size and shape. A moderate number of mitotic figures were present. There was a heavy infiltrate of lymphocytes in the wall of the ureter.

The kidney was not remarkable except for some hydronephrosis. Diagnosis: Papillary infiltrating transitional cell carcinoma grade 2; hydroureter and hydronephrosis.

Followup: The patient was discharged from the hospital on March 14, 1951 and readmitted 1 year later on March 5, 1952 at which time she had a recurrence of the tumor in the bladder involving the whole trigone and the anterior wall of the bladder, just above the vesical neck. A suprapubic cystotomy was done and the areas were resected with the loop electrode and the bases thoroughly coagulated. The patient was discharged on April 10, 1952. Microscopically, the tissue showed papillary infiltrating transitional cell carcinoma grade 2.

She was readmitted 2 months later, June 3, 1952, at which time three small papillary growths were found in the bladder. These were all coagulated cystoscopically.

Case 10 (fig. 13). Papillary infiltrating transitional cell carcinoma grade 3 of ureter.

J. C. G., a man aged 73, was admitted to Ste. Anne's Military Hospital on December 11, 1946 in an emaciated condition, complaining of a poor appetite of 6 months' duration, and a crampy left lower abdominal pain with nausea and vomiting of 1 months' duration.

Physical examination revealed a very thin emaciated man. The head and neck were normal. The heart and lungs were normal. Blood pressure 130/75.

The liver was markedly enlarged; the right lobe felt very firm and irregular;

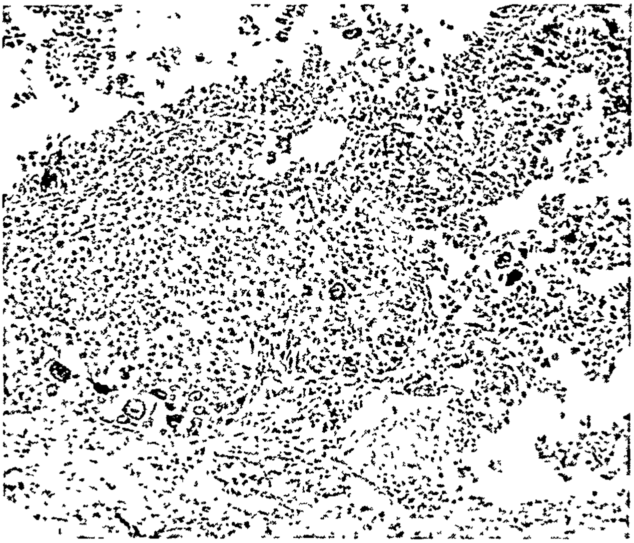


FIG. 13. Case 10. Microscopic section showing papillary transitional cell carcinoma grade 3, ureter. Note very large nuclei at base of tumor. Tumor extended through wall into periureteral fat in one area.

the left lobe could not be palpated. There was tenderness in the left lower quadrant of the abdomen, but no abnormal masses were palpated. Neither kidney was palpated. Genitalia were normal. Rectal: sphincter tone normal. Prostate: enlarged 1½ times normal size, fibroelastic, not fixed, not tender.

The patient died 3 days after admission to the hospital. An autopsy was performed. The essential findings are related below.

Autopsy findings: The right kidney weighed 89 gm.; 4 cm. of the ureter in its distal third was filled with a soft, friable tumor which encircled and invaded the wall. Small tumor nodules were present on the mucosal surface above and below the main growth. The ureter proximal to the lesion, and the pelvis were dilated.

Sections of the ureter showed a papillary tumor which extended through the wall into the periureteral fat. Cellular pleomorphism was marked.

The liver weighed 2980 gm. and the right lobe was almost completely replaced by metastatic carcinoma. There was also metastatic carcinoma in the para-aortic and iliac nodes. Diagnosis: Papillary infiltrating transitional cell carcinoma grade 3 of ureter; metastatic carcinoma in liver and lymph nodes (para-aortic and iliac); hydroureter and hydronephrosis; left kidney normal.

SECONDARY METASTASES TO URETER

In 1931 MacKenzie and Ratner reported 3 cases of secondary metastatic growths of the ureter. One was from an adenocarcinoma of the prostate and in 2 the primary growth was an adenocarcinoma of the stomach.

In the years 1932 to 1954 inclusive, there have been 10,223 successive autopsies at the Royal Victoria Hospital. In these 10,223 cases, secondary metastases of tumor to the ureter were found in 39 cases. Of these 39 cases, 18 had an actual lesion in the ureter, and 21 had a lesion surrounding the ureter and occluding it.

These 21 cases should not be considered as true metastatic lesions of the ureter Of the 18 cases in which there was an actual lesion in the ureter, the primary lesion was in the bladder in 6, in 3 the primary tumor was in the kidney, and in 2 the primary lesion was in the renal pelvis

This leaves only 7 cases in which the primary lesion was outside the urinary tract The other sites involved were adenocarcinoma of the prostate 1, carcinoma of the rectum 2, carcinoma of head and body of pancreas 1, carcinoma of breast 1, carcinoma of the thyroid 1, and a melanoma metastasizing to the kidney and ureter 1 These 7 cases give an incidence of true metastases in the ureter from a primary tumor arising elsewhere in the body, but outside the urinary tract, of 0 07 per cent

In the 21 cases in which the ureter was occluded by tumor surrounding it, the primary lesion was in the breast 2, ovary 2, cervix 10, rectum and sigmoid 4, lymphosarcoma of the jejunum 1, carcinoma of the prepuce 1, retroperitoneal lymphosarcoma 1 External occlusion of the ureter caused by metastases from a primary carcinoma elsewhere occurred in 0 20 per cent of the autopsies

ENDOMETRIOSIS OF THE URETER

Endometriosis of the ureter is included for completeness and because of the fact that it might be mistaken as a primary neoplasm of the ureter, as pointed out by Randall in 1941, when reporting the first case

O'Conor and Greenhill, in their excellent article on endometriosis of the bladder and ureter, reported a case of endometrioma of the urinary bladder, and another case of endometriosis of the ureter They also discussed the three main theories advanced as to etiology

There have been no known cases of endometriosis of the ureter at the Royal Victoria Hospital during the past 37 years

METHOD OF SPREAD OF TUMOR AND SITE OF METASTASES

Metastases from tumor of the ureter occur relatively early There may be a considerable degree of extension within the lumen of the ureter Extension through the thickness of the ureter occurs relatively early due to the thin walled nature of the ureter

When the lymphatics and the bloodstream are invaded, metastases may occur anywhere in the body The common sites encountered are the local lymph nodes, liver, vertebra, lung, kidney, spleen, pancreas and brain

METASTASES OF TUMOR TO THE RENAL PELVIS

Although secondary tumor metastases to the kidney are relatively common, metastases to the renal pelvis are quite rare

The authors wish to report a case in which a hepatoma in the liver metastasized to the left renal pelvis A staghorn calculus also was present in the renal pelvis (This case is being reported separately by Lingard, MacLean, and Heustis)

Case 11 (fig 14) Metastatic carcinoma in the renal pelvis from primary carcinoma in the liver

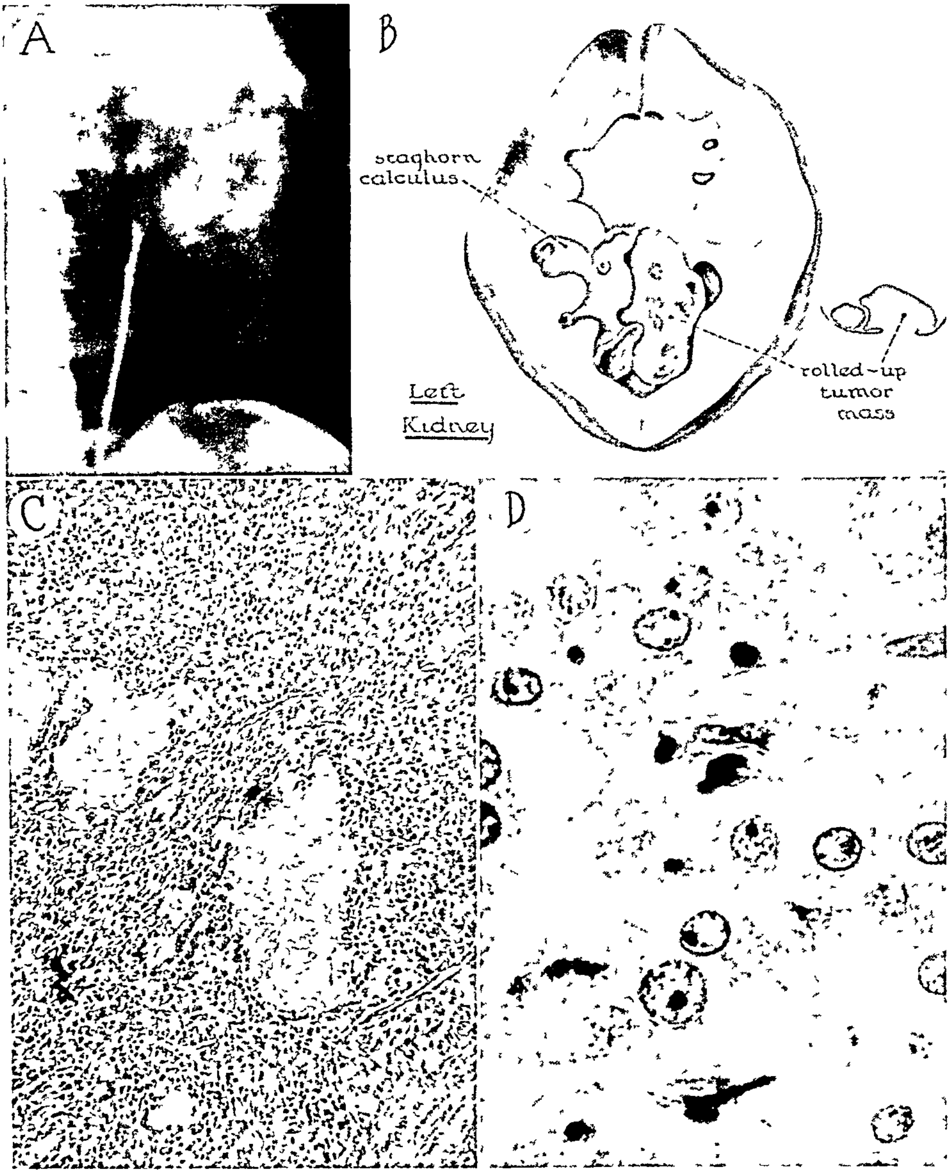


FIG. 14. Case 11. *A*, retrograde pyelogram showing filling defect in left renal pelvis and partial staghorn calculus. *B*, sectional drawing of kidney showing calculus and tumor mass in lower portion of renal pelvis. *C*, microscopic section of tumor showing cords of liver like cells, blood sinuses and lakes. *D*, microscopic section of tumor from renal pelvis showing bile plugs.

A 60-year-old Chinese man was admitted to the urology service of the Royal Victoria Hospital in May 1954 with the complaints of gross hematuria, dysuria, and weight loss of 18 pounds over the past 10 months. The past history and family history were noncontributory. Gross hematuria had been present 10 months ago, 4 months ago, and for the 2 weeks immediately prior to admission. The blood was mixed throughout the urine. During the past 8 months, the nocturia amounted to three to four times per night. Physical examination revealed some left loin tenderness Neither kidney was palpable The liver was not enlarged The prostate gland was about twice normal size, fibroelastic, not fixed, not tender There were no other palpable abdominal masses The urine was grossly bloody and contained clumps of pus cells The hemoglobin was 95 per cent and the nonprotein nitrogen was 19 mg per cent Cystoscopy revealed a normal lower urinary tract Retrograde pyelography showed the presence of a large staghorn calculus occupying the lower half of the left kidney and dilated calyces The right pyelogram was normal Nephrectomy on the left side was performed May 15, 1954

Pathological report The left kidney measured 11 by 5 by 3 cm The capsule was removed easily to show a smooth external surface On section there was loss of corticomedullary demarcation in multiple areas and some of the pyramids were hemorrhagic The calyces were moderately dilated and the internal surface of the pelvis was blood stained and roughened In the lower part of the pelvis was a dark reddish mass of tissue resembling blood clot measuring 5 by 2 by 2 cm This was loosely adherent to the internal surface of the pelvis Cut surface of this mass was grey with irregular hemorrhagic areas A staghorn calculus had been removed from the pelvis following nephrectomy It was composed of apatite 60 per cent and struvite 40 per cent

Sections of the kidney showed chronic pyelonephritis and in addition an acute inflammatory reaction with hemorrhage and necrosis in some of the pyramids and peripelvic tissues The epithelium of the pelvis was eroded in some areas Sections of soft tissue mass found within the pelvis showed it to be composed of columns of polyhedral epithelial cells separated by sinusoidal spaces filled with blood Golden brown, bile like plugs could be seen between the epithelial cells where they were arranged in solid groups The structure and cellular appearance definitely resembled liver tissue

Some sections through the renal pelvis in roughened areas showed the epithelium to be replaced by bile forming tumor cells There was no invasion of muscle or blood vessels Large blood lakes and areas of hemorrhage and necrosis were present in the tumor Only a few of the epithelial cells had abnormally large nuclei, no mitoses were present Some of the brown pigment gave a positive reaction with a histochemical test for bile and some of it gave a positive reaction for iron Diagnosis Metastatic carcinoma in the renal pelvis from a primary carcinoma in the liver Followup Two and one half months later, the patient was readmitted to the medical service complaining of anorexia of 3 weeks' duration and pain in the right upper quadrant of the abdomen In addition he had become jaundiced and was passing light colored stools

Physical examination revealed a cachetic man with markedly icteric sclerae Coarse rales were heard throughout the right lung and abdominal examination revealed a palpable liver 10 cm below the right costal margin The hemoglobin was 42 per cent and the white blood count 22,000 About four hours following admission the patient's condition deteriorated rapidly and he expired

Postmortem examination revealed the presence of primary carcinoma of the liver with multiple tumor nodules measuring up to 20 mm in diameter present in the lungs and adrenals The liver measured 22 by 26 by 10 cm and was greenish in color and friable in consistency. It weighed 2475 gm. A liver fluke infestation was found. Cholelithiasis and arteriosclerosis of the coronary arteries were concomitant findings. There was no tumor in the right kidney or in the lymph nodes.

SUMMARY AND CONCLUSIONS

Early in embryonic life, the bladder, ureter, and renal pelvis are lined with identical and continuous epithelium which is transitional in type. This explains why tumors arising in any of these areas are similar in type, and may be identical in histological appearance.

The effect of chronic irritation on the epithelium of the renal pelvis and ureter with resultant proliferative changes is discussed. Metaplasia to squamous epithelium or to mucin-secreting gland formation is discussed. A case showing mucinous metaplasia of the renal pelvis with mucin-secreting glands in the tunica propria is presented. This is a very rare type of case. Other cases showing proliferative irritative changes and squamous metaplasia are shown.

The significance of "predisposing factors" and of "seeding," in relationship to urinary tract tumors is discussed. The relationship of normally occurring steroids and of chemical carcinogens to the production of tumor in the urinary tract is noted.

There is a very high incidence of calculus present in tumors of the renal pelvis and ureter.

At the Royal Victoria Hospital, in the 30-year period from 1925 to 1954 inclusive, there were 4 cases of primary carcinoma of the ureter operated upon. In a 22-year period from 1932 to 1954, there has been 1 case of primary carcinoma of the ureter found in 10,223 successive autopsies. In the 8-year period from 1946 to 1954, in the Department of Veterans Affairs Hospitals in Canada, there have been 6 cases of carcinoma of the ureter operated upon, and 1 found at autopsy.

In the 15 years, 1917 to 1931, at the Royal Victoria Hospital (as reported by MacKenzie and Ratner) there were 96 cases of renal tumor operated upon, only 1 of which was a case of tumor of the renal pelvis. In the following 23 years from 1932 to 1954, there were 111 kidney tumors operated upon, of which 14 had primary carcinoma of the renal pelvis. In the 8-year period, 1946 to 1954, the Department of Veterans Affairs Hospitals in Canada had 164 cases of tumor of the kidney operated upon or found at autopsy, of which 18 were carcinomas of the renal pelvis. In the total series of 471 cases of kidney tumor, 33 were carcinomas of the renal pelvis, giving an incidence of 7 per cent.

Typical cases of tumor of the renal pelvis and ureter are presented, along with the microscopic sections. In addition, a case of squamous cell carcinoma of the renal pelvis and a case of an infiltrating squamous cell carcinoma of the renal pelvis containing mucin-secreting glands and cells are shown.

A case of metastases of a primary carcinoma of the liver to the left renal pelvis is presented. It was associated with a staghorn calculus.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

THE DIAGNOSIS OF TUMORS OF THE RENAL PELVIS AND URETER

VINCENT J. O'CONOR

In recent years, there has been a marked increase in the incidence of tumors arising primarily in the renal pelvis and ureter. There is sufficient evidence to prove that this recognition has not been due entirely to improved, or more universally applied, diagnostic procedures.

Just as the geographic incidence of papillary tumors of the bladder has followed the aniline-dye industry around the world, so also the increased finding of similar tumors arising in renal pelvis and ureter suggests a more common exposure to some sort of urinary carcinogen encountered in the daily routine of our present life. The occupational hazard of exposure to the aniline-dyes and various other petroleum derivatives is well recognized and is universally accepted as one of the two known specific causes of transitional-celled tumors of the urinary bladder. The other known specific etiologic agent in the production of bladder neoplasm is infection with Bilharzia (schistosomiasis).

During the past few years a number of carefully-controlled research projects in the dog, conducted separately in several English and American clinics, have conclusively demonstrated the carcinogenic effects of B-naphthylamine and allied products in the production of bladder tumors of a papillary nature. These excellent investigations have further shown that these carcinogens, if we may use that term loosely, are specific for the transitional-celled lining of the urinary tract and require, in addition to direct contact, something of a time element in this actual apposition to the mucosa. Lack of development of tumor in any portion of the bladder which has been marsupialized or removed from contact with the urine; development of tumors in the ureter or renal pelvis of the dog only after partial obstruction to the ureter has resulted in the urinary stagnation associated with hydroureter and hydronephrosis.

Therefore, the most important point in considering the subject of the diagnosis of tumors of the renal pelvis and ureter is the necessity to realize the relative frequency with which they may be encountered. Those of us who have been especially concerned with lesions of the urinary tract over a period of many years have probably learned this fact the "hard" way. As a result of our considering these tumors to be rare, stones have been removed from the ureter and renal pelvis without recognizing the fact that they were associated with small primary neoplasms. Many hydro- or pyonephrotic kidneys have been removed with portions of the ureter which were above the point of obstruction due to the primary ureteral tumor.

During my period of training at the Peter Bent Brigham Hospital, we encountered two instances of primary tumor of the renal pelvis and one tumor arising in the lower left ureter. This latter was considered unusual enough to form the basis of a report before this society by William C. Quinby in 1922.

In pursuing my interest in the subject of primary tumor of the ureter some

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Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23–25, 1955.

years ago, I recall a statement made by someone to the effect that in the first one hundred years of operation of the Massachusetts General Hospital only one instance of primary neoplasm of the ureter was recorded Compare this incidence to the fact that some 20 years ago a urologist from a relatively small clinic in Wisconsin reported eight authentic cases in which a preoperative diagnosis had been made

Since my assignment in this symposium limits my discussion to "diagnosis," I can best be brief and mention only the points which our own experience seems to emphasize as important

Since July 1, 1942, on our service at the Chicago Wesley Memorial Hospital in Chicago, we have found 33 instances of primary tumor of the renal pelvis Twenty-eight of these tumors were papillary (transitional-celled) in type and five were "solid" (squamous celled) In the papillary tumors, eight had neoplastic involvement of the ureter also Nine had papillary tumors of the bladder discovered at the original examination Two other patients, upon whom nephroureterectomy was performed, were subsequently found to have tumors in the bladder Thirteen primary tumors of the ureter, without evidence of renal involvement, were found Eight patients with "ureteral stump" tumor involvement after nephrectomy were encountered Seven of these had had nephrectomy elsewhere In six of these patients, the data we could obtain seemed to indicate that no primary growth had been found in the removed kidney A patient of our own, seen as recently as 1952, at which time I removed a large hydronephrotic kidney, returned in 1954 with gross hemorrhage from the ureteral stump Excision of the ureter disclosed the presence of multiple low grade papillary tumors which had undoubtedly been present as the cause of obstruction at the time of the original operation Up to this date, there has been no bladder involvement in this patient

Five of these 21 "primary" tumors of the ureter were flat, infiltrating squamous celled growths All had produced marked hydronephrosis with secondary infection in the ureter and kidney These tumors spread early and all were found to have regional or distant deposits The true nature of the "solid" tumor of the ureter is more difficult to diagnose preoperatively than is the case with papillary tumors The lesions to be confused with primary tumors of the renal pelvis and ureter are those which cause mechanical obstruction, calculus formation, infection and gross hematuria, in other words, almost all the pathologic conditions which can arise in these structures

Every patient presenting himself with papillary tumors of the bladder should be suspected of a similar type of lesion in one or the other urinary tree Cystoscopic examination may show tumor projecting from the ureteral orifice as it did in eight of our patients Radiographic study of the outline of the renal pelvis and ureter is, of course, necessary to arrive at a presumptive or positive diagnosis The filling defect due to tongue like protrusions of clear celled carcinoma of the kidney into the renal pelvis has prompted a diagnosis of primary pelvic tumor on several occasions Fresh or organized blood clots, "soft" or nonopaque calculi and necrotic renal papillae may provide pyelographic data simulating tumor of the renal pelvis Wherever possible, attempts to outline the entire ureter in case of extensive hydronephrosis may show a filling defect which would otherwise have been overlooked. If one is unable to outline the ureter and renal pelvis by excretory urography, and at the same time a catheter cannot be passed, it will be impossible to make a preoperative diagnosis. The only exception to this will be the finding of tumor cells in the urine, in which case it may be presumed that they have come from the obstructed ureter or renal pelvis. Up to now, these tests have not been helpful to us, but increasing technical skill in the future may prove such a search more worthwhile.

CONCLUSION

There seems to be definite evidence to prove that tumors of the renal pelvis and ureter are occurring more commonly than in the past. This trend will only be reversed when we identify the carcinogen, which we presume to be present in the urine. We will then take steps to eliminate or neutralize it All patients with papillary tumors of the bladder should be suspected of upper tract involvement also, even though the percentage of positive findings will be small.

Modern diagnostic measures, plus a recognition of the possibility that neoplastic lesions may suggest stricture, stone, blood clots or other necrotic tissue will lead to a more ready recognition of the true condition.

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The Journal of Urology
Vol 75, No 3 March 1956
Printed in U S A

PROGNOSIS OF PRIMARY TUMORS OF RENAL PELVIS AND URETER

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After reviewing the recent literature on primary tumors of the renal pelvis and ureter and their prognosis, I find that the subject does not lend itself well to statistical analysis The clinical material is so varied, and tabulated in such different ways, that one is unable to tell exactly how many of each type of tumor have been reported, nor how many have had either nephrectomy or nephroureterectomy with or without excision of a segment of the bladder The number of patients who have lived 1, 3, 5, or 10 years without recurrence cannot be accurately determined In addition, it is impossible to determine from many of the recorded reports whether the individuals were potentially curable by surgery because of inadequate information about the presence or absence of metastases or local extension at the time of operation There is also no uniformity in pathological descriptions, nor in the followup studies These are not faults of the capable authors who have recorded their findings nor inadequacies in their methods of studying the patient They are inherent variables in a complex problem Rather than to attempt a tabulation of all the reported series for this symposium it has seemed to me that a more profitable approach is to select for discussion, a few of the carefully studied and followed groups of patients and to report our own experience

To illustrate the difficulty in comparing the larger reported series of patients is the excellent report of Scott in 1943 on 149 patients with primary carcinoma of the ureter who were operated upon Thirty two patients were reported well when last seen, but of these only 6 were observed for more than 4 years In 182 cases of primary tumor of the ureter which he collected, there were 22 different pathological diagnoses and considerably more than 12 different kinds of operation The next similar report by Senger and others in 1953 analysed an additional 130 cases of their own and from the literature Fifty two of this collected group had shown no evidence of recurrence, but of these, 50 per cent had been followed for less than 1 year This again emphasizes the difficulty in establishing prognosis even from such an impressive collection of cases

A possible exception to the foregoing is the prognosis of squamous cell carcinoma of the renal pelvis or ureter The results of treatment are so uniformly poor in this condition that no long period of followup is usually necessary to know what happens to the individual patient In 1949 Gahagan collected 196 cases of squamous cell carcinoma of the renal pelvis from the literature and found no 5 year cure reported Since then cases reported by Oberkircher, Riches, and the 4 cases to be reported herewith bring the total to at least 275 In none of these

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Read at annual meeting, American Association of Genito Urinary Surgeons, Pebble Beach Calif May 23 25 1955 additional cases has a 5-year cure been reported. It would seem probable that this currently hopeless prognosis of squamous cell carcinoma of the upper urinary tract is due to the fact that these tumors produce symptoms late in the course of the disease. Silent hematuria is by far the most common early symptom of all urothelial tumors while pain or symptoms of infection or obstruction appear later. Papillary tumors characteristically produce luxuriant growth within the lumen of the pelvis or ureter and the trauma from peristalsis produces gross hematuria quite early as a rule, often before significant spread has occurred. Bleeding from squamous cell carcinoma, on the other hand, is late and is usually due to necrosis secondary to invasion and obstruction of nutrient blood vessels. Furthermore, these tumors are apt to be of a high degree of malignancy from a histological and biological standpoint as opposed to the slight evidence of malignancy seen in some of the transitional cell tumors.

Riches has recently reported 147 operable cases of transitional cell carcinoma of the renal pelvis collected in Great Britain. Of 79 cases with no involvement of the ureter or bladder, 62 per cent survived for 1 year and 41 per cent for 10 years. Of the 68 cases where the ureter or bladder was involved, although 71 per cent survived for 1 year, only 33 per cent survived for 3 years. Accordingly, he felt that involvement of the ureter or bladder made the prognosis of a primary carcinoma of the pelvis much more grave. Of 61 cases of benign papilloma of the renal pelvis which were followed for more than 1 year after nephroureterectomy 95 per cent survived for 1 year, 87 per cent for 3 years, and 50 per cent for 10 years. Perhaps the best results obtained to date are those reported by O'Conor with 8 of 12 cases of papillary carcinoma of the pelvis surviving without evidence of recurrence for from 4 to more than 10 years after operation. In contrast, Foot reports that of 19 patients who had nephrectomy for transitional cell carcinoma of the pelvis, only 1 lived for 5 years after operation and he died of cancer in the seventh year.

A most interesting report on 33 cases of primary carcinoma of the ureter from

TABLE 1. *Results of treatment of primary tumors of renal pelvis and ureter*

	Years after Operation								
	0–1	1–2	5–6	6–7	7–8	14–15	17–18	Total	
Transitional cell ca. of pelvis									
Living			1	1*	1		1	4	10
Dead	5	1						6	
Squamous cell ca. of pelvis									
Living		1						1	2
Dead	1							1	
Benign papilloma of pelvis									
Living					1	1		2	2
Dead								0	
Transitional cell ca. of ureter									
Living	4							4	8
Dead	1	3						4	

* Recurrent tumor present.

the Mayo Clinic has recently been made by Whitlock and others Of this group, 17 were purely superficial without involvement of the submucosa although histologically of varying degrees of malignancy Of those operated upon more than 3 years previously, 81 per cent survived, and of those operated upon more than 5 years previously, 66 per cent survived Of the 16 remaining patients in this group whose tumor showed infiltration of the ureteral wall only one survived for more than 3 years and he had extensive carcinoma at the time of his last examination Six of O'Conor's 8 cases of primary papillary tumor of the ureter survived from 2 to 11 years after operation, but the pathological findings in these cases are not described

The results of treatment of 22 patients with primary tumors of the renal pelvis or ureter at Duke Hospital are depicted in table 1 Four cases of transitional cell carcinoma of the pelvis are living for almost 6, 7, 8, and 18 years respectively since operation, although the 7-year survivor had recurrent tumor present in her bladder when last examined To re emphasize the difficulty in prognosis it is interesting to note that at the time of operation, the 18 year survivor operated upon by my associate, Dr E P Alyea, had a large mass of tumor extending down the lumen of the renal vein to its junction with the vena cava There was another tumor thrombus in the spermatic vein, and invasion of the renal parenchyma from the renal pelvis to, but not through, the capsule Five patients died within 1 year after operation and another within 2 years Of 2 cases of squamous cell carcinoma of the pelvis, 1 is living less than 2 years postoperatively and 1 died within 1 year after operation The 2 cases of benign papilloma of the pelvis are living for 8 and 15 years postoperatively, with no evidence of recurrence Each had simple nephrectomy Of 8 cases of transitional cell carcinoma of the ureter, 4 were last known to be living but for less than one year after operation Two of these have been operated upon within the last year whereas the other 2 could not be followed The remaining 4 are known to be dead in less than 2 years after operation

The results in untreated patients with primary pelvic tumors are shown in table 2, the diagnosis being made either at autopsy or at palliative operation Three patients with transitional cell carcinoma died within 1, 3, and 4 years respectively, and 2 patients with squamous cell carcinoma died within 1 and 2 years respectively, after the onset of symptoms

TABLE 2 *Results in untreated primary tumors of renal pelvis**

	Years after Onset of Symptoms				
	0–1	2–3	3–4	Total	
Transitional cell ca of pelvis					
Living				0	3
Dead	1	1	1	3	
Squamous cell ca of pelvis					
Living				0	2
Dead	1	1		2	

* Diagnosis at autopsy or palliative operation

The Journal of Urology
Vol. 75, No. 3, March 1956
Printed in U.S.A.

LOCALIZED AMYLOIDOSIS OF THE URETER: REPORT OF A CASE

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Localized amyloidosis of the ureter is a rare condition. Lehmann[1] reported the first case in 1937, discovered at autopsy on a 67-year-old woman. In 1952, Gilbert and McDonald[2] reported the second case (the first in English literature), a 52-year-old white woman, on whom left nephrectomy was performed for hydronephrosis and left ureteral obstruction. In their case the lower calyx, inferior portion of the renal pelvis, and 3.0 cm. of the ureter were involved by amyloidosis.

We are reporting the third case of localized amyloidosis of the ureter.

CASE REPORT

A 71-year-old white woman, never in good health since the age of eleven, with a multitude of recurring allergic, gastrointestinal, circulatory, and other complaints, experienced a sudden high temperature, pyuria, and pain in the right lumbar region which responded poorly to antibiotic therapy. One such attack 3 months previously responded poorly to treatment. The history included a diagnosis of granulative urethritis 9 years ago, treated by urethral dilatations. A retrograde pyelogram at that time was not remarkable (fig. 1, *A*). Cystoscopic and radiographic studies demonstrated a normally functioning bladder and left kidney, and marked right hydronephrosis and hydroureter due to organic obstruction of the right ureter about 3 cm. from the bladder (fig. 1, *B*). A right nephroureterectomy was performed, followed by normal convalescence.

Pathological report: The gross specimen was a 13 by 9 by 4 cm. kidney with 20 cm. of ureter attached. The latter, averaging 1.5 cm. in diameter, was obstructed 2.0 cm. proximal to its surgical margin by a 2 by 1 by 1 cm. firm, tan mass that uniformly involved the ureteral wall. The dilated renal calyces and pelvis contained grossly purulent material.

Microscopic description: The ureteral mucosa was focally lined by transitional epithelium with scattered, shallow ulcerations. The propria was diffusely infiltrated by lymphocytes, plasma cells, macrophages with foamy cytoplasm, and scattered neutrophils. There were scattered foci of necrotic cellular debris. In the mucosal propria, and largely obliterating the muscularis, were sheets and ovoid deposits of palely eosinophilic, homogeneous material. These deposits occasionally lay beneath the endothelium of small blood vessels. Rare multinucleated giant cells bordered the deposits. See figure 2. Peripherally, lying within the adventitia, was a rim of irregular bone trabeculae with foci of osteoid tissue that occasionally lay immediately adjacent to, but appeared demarcated from, amyloid deposits (fig. 3). The bone trabeculae often encased fatty stroma,

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Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23–25, 1955.

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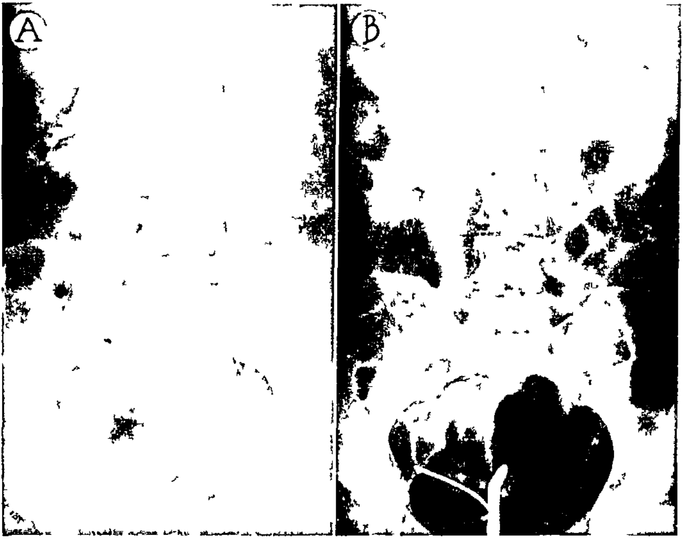

FIG 1 A, retrograde pyelogram 1945 Essentially normal *B*, retrograde pyelogram 1954 *Tiny, hair sized channel runs upward toward greatly dilated, tortuous lower right ureter, indicating annular constriction of lower ureter*

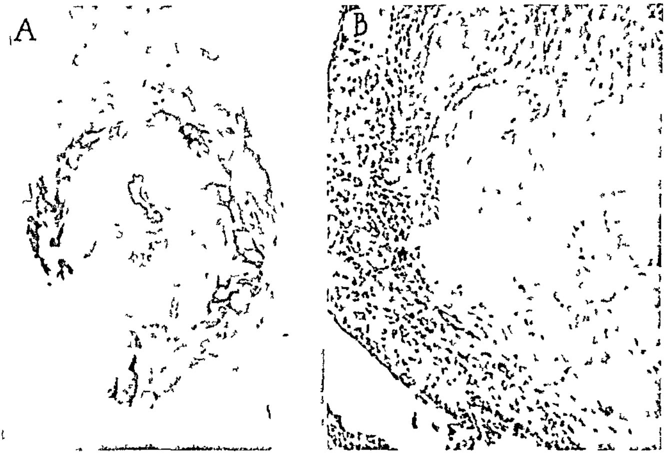

FIG 2 Cross section of ureter showing a slit like lumen, replacement of wall by amyloid, and peripherally located bone trabeculae *B*, ureteral lumen at upper left, with underlying amyloid deposit

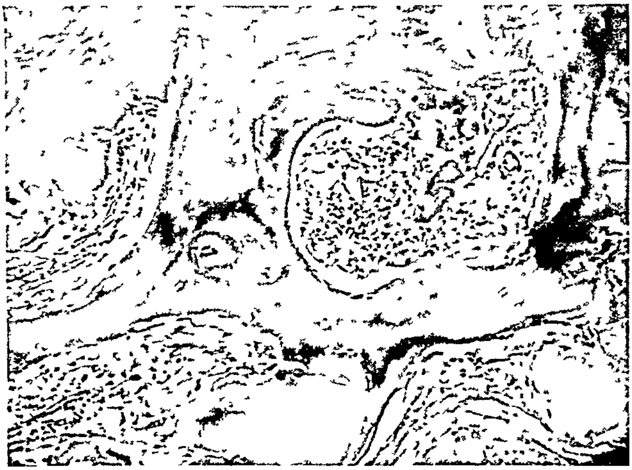

FIG. 3. Detail of bone formation with apposed amyloid deposits

but marrow cells were not identified. Sheets of amyloid frequently lay within these intertrabecular spaces, along with light infiltrations of lymphocytes and plasma cells. Rare osteoclasts were noted. In the adventitia homogeneous eosinophilic deposits occasionally bordered vessels, both subintimal and perivascular in location. With Congo red stain, these deposits appeared light orange to orange red. In a crystal violet stain they presented an uneven reddish purple hue.

Kidney sections exhibited focal interstitial infiltrations of lymphocytes, plasma cells and neutrophils in both cortex and medulla. Clusters of neutrophils lay within scattered tubule lumina. There was some clustering of glomeruli. The pelvic mucosa was focally ulcerated and heavily infiltrated by acute and chronic inflammatory cells. No acid-fast bacilli were seen in Ziehl-Neelsen stains of kidney and ureter.

Diagnosis: Localized amyloidosis, right ureter, with granulomatous inflammation and osseous metaplasia; hydronephrosis and subacute pyleonephritis, right.

Pre- and postoperative laboratory studies: Red blood cells, 4,200,000; hemoglobin, 12 gm.; white blood cells, 9,000. Differential: 6 stabs, 89 polys, 4 lymphs, 1 eosin. Blood Wassermann: Negative. X-rays of the chest and gastrointestinal tract were normal. A Congo red test revealed 30 4 per cent absorption of the dye, a normal result. Calcium, 9.2 mg. per cent; alkaline phosphatase, 2.5 units (Bodansky); total protein, 6.75 gm. per cent; albumin, 4.47 gm. per cent; globulin: 2.28 gm. per cent; A/G ratio, 1.96. The urine was negative for Bence-Jones protein. Bone marrow aspiration was refused.

DISCUSSION

The classification of amyloidosis as 1) secondary, 2) primary, 3) associated with multiple myeloma, and 4) localized, has been generally accepted. It is, however, of interest that in a recent report Wolf et al.[3] have questioned the validity of sharply segregating amyloidosis into distinct types. They reported a case of amyloidosis, unassociated with a predisposing disease, presenting features of primary, secondary, and localized amyloidosis. However, to date in our case we have found no evidence of amyloid deposition other than in the ureter. The similarity of the clinical features of the case reported by Gilbert and McDonald and our own is striking, indicating the advisability of considering localized amyloidosis in the differential diagnosis of ureteral obstruction. Whether or not previous ureteral inflammation is a factor in the pathogenesis of this condition is uncertain. In our case there was history of previous urinary tract infection. Possibly the inflammatory reaction associated with the amyloid deposit was secondary. Bone formation, prominent in the ureteral adventitia of our case, is also described in Lehmann's report.

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SUMMARY

A case of localized amyloidosis of the ureter with secondary hydroureter and hydronephrosis is reported, and is the third instance of this condition recorded in the medical literature.

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

SMOOTH MUSCLE REGENERATION IN REPAIR OF EXPERIMENTAL URETERAL DEFECTS: THE SIGNIFICANCE OF THE DOUBLE LUMEN

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Regrowth of the ureteral wall after partial resection has been studied experimentally by several workers[1-7] to determine the conditions for repair in Davis' intubated ureterotomy. The mucosa is found to be replaced within a week, and the muscle within 4 to 6 weeks.

Recent experimental work in our laboratory[8] indicated that actual growth of smooth muscle can occur, especially from the cut edges, although reconstitution is probably hastened by fibrous contracture of the scar tissue. Since the present report is on a continuation of that study, the principles and technique will be reviewed:

In order to separate the force of circular contracture of the fibrous tissue which is initially laid down to bridge the defect, from the factor of actual new growth of smooth muscle, a wire mesh fixed in a polyethylene splint (fig. 1) was laid across the cut edges. This prevented fibrous contracture, so that any muscle found beyond the barrier at the end of the experiment would necessarily have arrived by actual regeneration of the muscle fibers.

Sections made after from 6 to 12 weeks showed varying degrees of new muscle growth, but in all specimens in which the initial area of regeneration could be identified, it uniformly lay adjacent to the normal muscle on the other side of the barrier (fig. 2).

PRESENT EXPERIMENTAL STUDY

An incidental observation in the previous experiments was that fibrous tissue would grow along the barrier in certain instances, thereby forming a double lumen. Specimens showing this phenomenon form the basis for the present study.

Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23–25, 1955.

Supported by the Edwards Fund for Medical Research.

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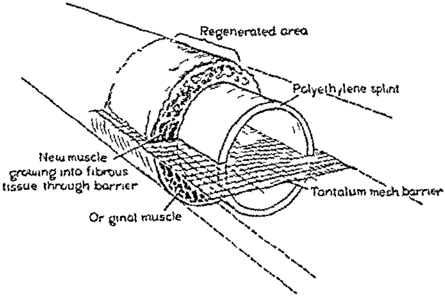

FIG 1 Schematic drawing of experiment, showing relation of normal smooth muscle to newly regenerated muscle Fibrous contracture is prohibited by wire barrier Stippled area is site of 1) excision of ureteral wall, 2) laying down of initial fibrous tissue, as normal step in healing process, and 3) ingrowth of smooth muscle from cut edges.

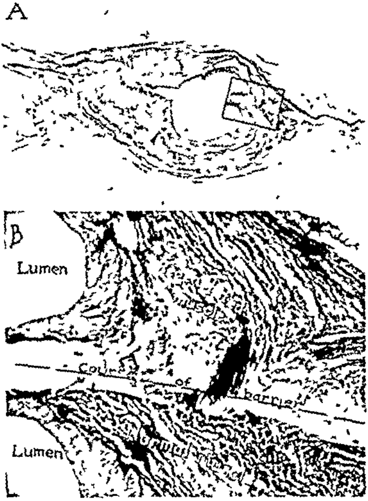

FIG 2 A, cross section of ureter, No 86E, 11 weeks after operation Site of barrier is seen in B, with normal muscle below and tongue of new muscle growing into fibrous tissue above

TABLE 1

Degree of Smooth Muscle Regeneration	Dog #	Weeks P O	Remarks
Minimal (±)	165	6	
	200	8	Ureter fell entirely away from splint
Moderate (3+)	110	9	
	86C	11	Control area with partial formation of double lumen
Complete (4+)	176	8	
	11	8	

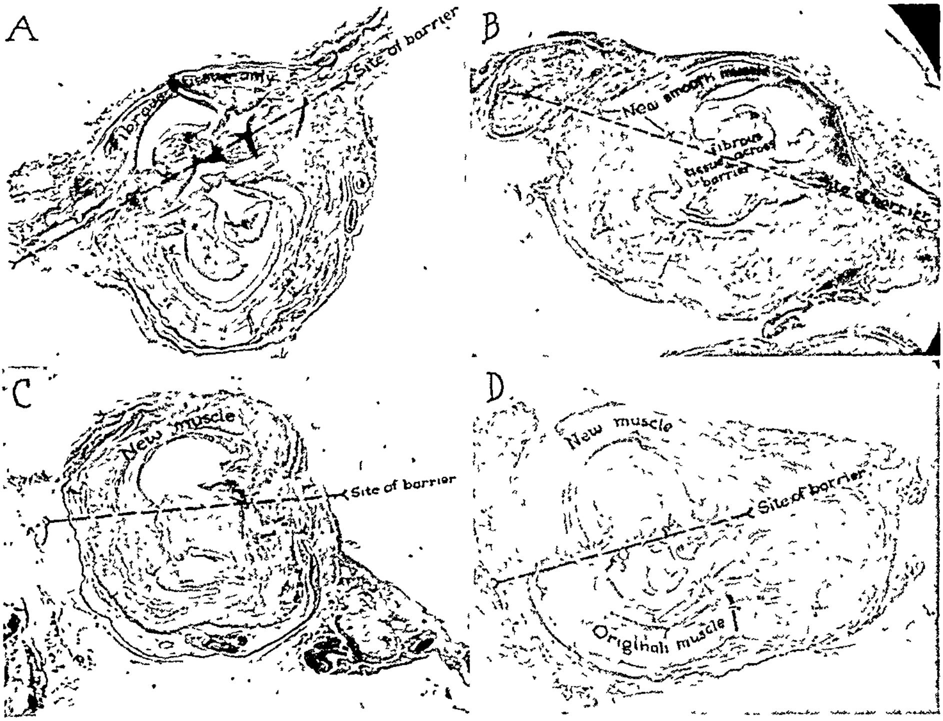

FIG. 3. Cross sections of ureters with incomplete double lumens. *A*, No. 165A; *B*, No. 110; *C*, No. 176 and *D*, No. 14. Note absence of new smooth muscle in *A*, but ingrowth of muscle in *B*, into new wall and into area of barrier.

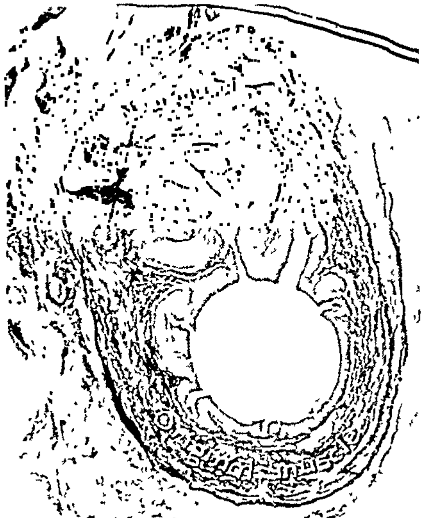

FIG. 4. Cross section, No. 86C. No barrier present in this area but ureteral mucosa and wall have fallen partially away forming a redundancy (early double lumen formation).

Six specimens were prepared by the technique described in the earlier communication, and representative cross sections studied. All ureters had two lumens on section (table 1). In four specimens (165, 110, 176, and 14), the double lumen resulted from growth of the initial fibrous tissue along the wire barrier. Epithelium lined the outer lumen and smooth muscle grew into the new wall in varying degrees (fig 3) Of significance is the fact that it grew also, although to a lesser degree, into the fibrous tissue lying across the wire barrier (fig 3, *B*)

In one specimen, 86C, the wall of the defect had been drawn partially away, so that a sacculation was formed (fig 4), a transition stage to true double lumen formation However, because the margins of the cut ureter remained open, new muscle growth continued from the cut edges

One specimen (No 200) showed the most complete luminal reduplication The ureter, after one half its wall was resected, did not remain in apposition

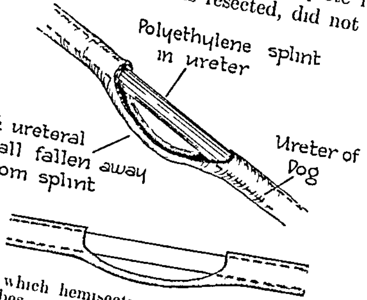
Polyethylene splint in ureter
½ ureteral wall fallen away from splint
Ureter of Dog

FIG 5 Mechanism by which hemisectioned ureter falls away from splint allowing healing as two separate tubes

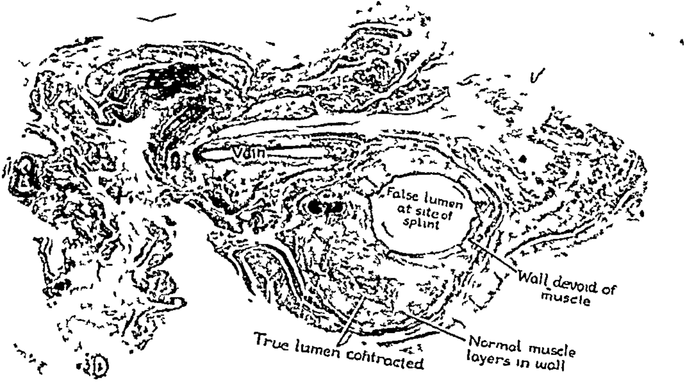

FIG 6 Cross section of specimen No 200 False lumen has been created about splint leaving cut edges of ureter to draw together and reconstitute original lumen Note that new ureteral wall is devoid of smooth muscle, apparently since a free cut edge of ureteral muscle was not present from which growth could start

with the splint, but fell away (fig. 5). Its cut edges then simply reapproximated themselves leaving a slight scar and a small lumen. The significant fact is that no muscle is seen in the walls of the new "ureter" (fig. 6). The bundles of the normal ureter pursue their usual course without deviation or extension into the area of the new lumen. The meaning of the absence of muscle growth under these conditions is the subject of this discussion.

The question was raised during our studies as to whether the double lumen was actually a second ureter or merely one of the cystic spaces described by Trautner and Raaschau.[5] However, in the present experiments, the lumen was determined to be continuous with the ureter by dissection, since the splint in each case was withdrawn from the lumen.

SUMMARY OF EXPERIMENTAL FINDINGS

Smooth muscle can be seen to grow from the cut edges of the ureter when circular contraction is prevented by interposition of a wire barrier. Similarly, even if fibrous tissue grows across the barrier, forming two lumens, the muscle grows (although at a slower rate than the epithelium) into the septum.

If, however, the open hemisection of ureter falls away from the splint, its edges coapt, reforming the cylindrical structure, as would be expected from the experiments of Davis and others already cited. The adjacent fibrous tissue forms a sturdy wall about the nearby splint, but this new "ureter" is not invaded by smooth muscle bundles.

The formation of a second ureter has been described before as a complication of experimental intubated ureterotomy. However, double lumen formation provides an important link in the evidence that the site of regeneration of smooth muscle after resection of a part of the circumference of the ureter is from the cut edge of normal ureter.

SUMMARY AND CONCLUSIONS

An experimental technique was used to prevent healing by fibrous contracture of the ureteral defect in intubated ureterotomy, by interposition of a wire barrier. Actual smooth muscle regeneration has been observed and recorded.

Partial reduplication of the lumen occurred if fibrous tissue grew along the barrier. The septum was invaded by smooth muscle.

A complete second ureter was formed in one experiment in which the unroofed ureter fell away from the splinting catheter. The wall of the false lumen about the splint contained no muscle, the ureteral edges having healed together, leaving no exposed edge of muscle. Since no source for regeneration of new muscle was provided and no muscle growth occurred, there is reason to believe that smooth muscle regeneration after intubated ureterotomy occurs principally from normal ureteral wall. Perhaps it might follow that the more normal the initial ureteral musculature, the better the quality and quantity of the regenerated muscle.

These experiments add evidence to our previous observation that the smooth muscle of the ureter regenerates, arising in the main from the cut edge of normal muscle.

THE JOURNAL OF UROLOGY
Vol 75 No 3, March 1956
Printed in U S A

DIAGNOSIS OF UROLOGIC COMPLICATIONS IN GYNECOLOGY

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The most common complications occurring during pelvic surgery on the female are the result of trauma to the urinary bladder or ureters Injury to the bladder is often recognized at the time of surgery and repaired When a urinary fistula develops postoperatively, a urologist may be consulted relative to the diagnosis and treatment, however, it is generally considered a gynecological problem

The literature contains many reviews of the frequency of ureteral injury during extensive pelvic surgery The incidence of this tragic happening is clothed by devious factors, so that many have been unreported, unrecognized, and often unrevealed because of the paucity of symptoms

Since the generally accepted incidence of surgical injury to the ureter is relative and the arbitrary figure not entirely accurate, too great reliance cannot be placed on the frequency with which the condition has been encountered as a sequel of surgery The occurrence of ureteral ligation as a complication of all operations on the female genital organs has been estimated as much as 3 per cent The relative ratio of unilateral to the bilateral injury is presumed to be 6 to 1 The morbidity ratio of the past can be hardly comparable to that which existed prior to the institution of the various sulfa drugs and antibiotics, the complications, independent of infection, still tax the ingenuity of the surgeon and re-emphasize the great importance of all preventive measures A decided interest has developed during the past years in a more general and better understanding of all the principles which contribute to the prevention and correction of ureteral damage Much of this has come about as a result of the experience of the war

Abdominal surgical procedures have been regarded as the most frequent cause of ureteral trauma However, the instances of injury to the ureter occurring during gynecologic operations have been more common recently due to the increasing use of panhysterectomy both in benign and malignant pelvic conditions

The most common site for ureteral injury has been repeatedly noted by various surgeons Novak described five danger zones in the female patient as follows

1) Where ureter crosses the iliac vessels
2) Ovarian fossae
3) Intraligamentary portion of the ureter
4) Where ureter is crossed by the uterine artery
5) Intravesical ureter in the repair of vesicovaginal fistula

The most skilled and experienced gynecologist may inadvertently cut or ligate one or both ureters in a hysterectomy, if it is unusually complicated or difficult The urologist is consulted when complete anuria or persistent flank pain follows

Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach Calif May 23-25, 1955

such a procedure as removal of diseased fallopian tubes or intraligamentous cysts, vesical tumor, or carcinoma of the uterus. The usual types of injuries are ligation, incision, resection, clamping and extensive stripping of the ureter with interference of the blood supply.

The general symptoms of rupture or penetration of the ureter include pain along the course of ureter and muscle spasm, intermittent chills and fever, though these may not appear until some time after the operation when infection or toxic absorption from extravasated urine has had a chance to be effective. At first there may be nausea and vomiting, which usually cease after 24 hours. The patient lies in bed with the leg of the affected side drawn toward the abdomen in an attempt to relieve the contraction of the irritated iliopsoas muscle.

The early physical findings of ureteral ligation or marked angulation producing obstruction are abdominal distention and flank pain. Renal manifestations in some instances may remain in a quiescent state for months or even years before hydronephrosis, pyonephrosis, or complete atrophy of kidney develops. When the renal duct has been traumatized by needle puncture, incision, segmental resection or necrosis from application of clamps or extensive stripping, and an intraperitoneal urinary extravasation occurs causing acute peritonitis, death may result within a few days. More often, however, the urine finds its way to the surface by the formation of a ureterovaginal fistula, or drainage of urine from the abdominal wound. When both ureters are ligated, absolute anuria is present from the time of surgery.

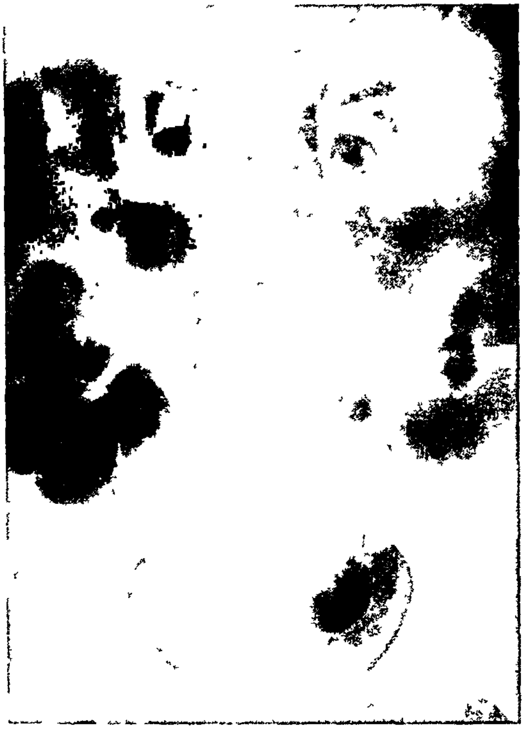

FIG. 1 Case 1. Excretory urogram demonstrates severed left ureter and extravasation. Accident occurred during operative removal of intraligamentous cyst.

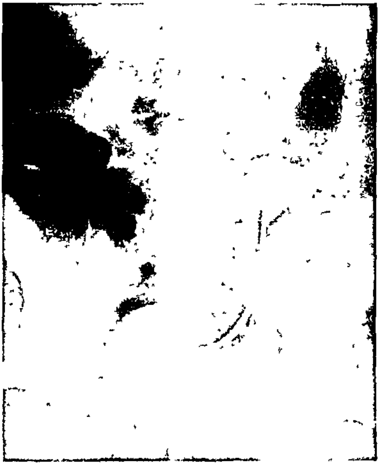

FIG. 2. Case 2. Attempted left ureteral catheterization on eleventh postoperative day Faulty ureteral union was demonstrated by obstruction and extravasation.

When injury to a ureter is recognized at the time of surgery, it should be repaired immediately, preferably over an indwelling ureteral catheter as a splint. Occasionally, difficulty is encountered in locating the severed ends of the traumatized duct. An investigation which requires but a few minutes is the intravenous use of indigo carmine to locate the proximal portion, and the passage of a ureteral catheter to identify the distal end of the ureter.

When symptoms develop postoperatively suggesting injury to the ureter, the use of excretory urograms, cystoscopy, and the retrograde introduction of ureteral catheters will always locate the area of obstruction, and frequently the extent of damage to the renal duct.

I would like to illustrate and in this way re-emphasize the value of our diagnostic aids in patients with ureteral injury:

Case 1. R. A., a woman aged 39, had a large intraligamentous cyst removed. The day following surgery, the patient complained of abdominal pain and distention. Urinary drainage came from the abdominal wound. On the fifth postoperative day, excretory urograms disclosed a severed left ureter and extravasation (fig. 1).

Case 2. P. E., a woman aged 60; diagnosis, intraligamentous cyst of the left ovary. During the removal the left ureter was cut. The ureter was immediately repaired by end-to-end anastomosis over a No. 8 catheter. The catheter was removed 10 days later. The patient experienced severe abdominal pain and rigidity. Attempted ureteral catheterization on the eleventh postoperative day revealed faulty ureteral union and extravasation necessitating nephrectomy (fig 2).

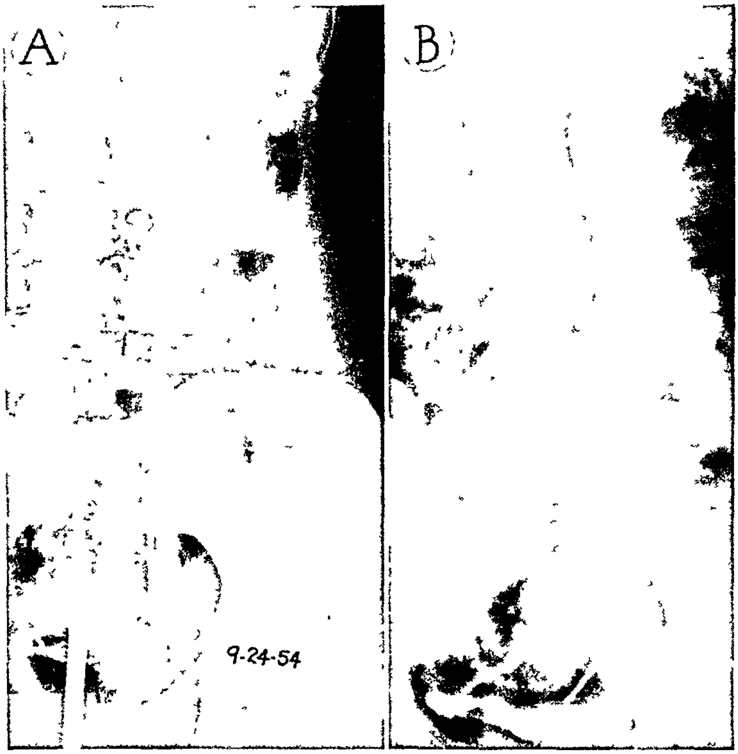

FIG. 3. Case 3. *A*, one month postoperative retrograde urogram demonstrates normal ureter and moderate hydronephrosis. *B*, enlarged left renal shadow. Obstruction of catheter in pelvic ureter without extravasation. Opaque medium returned around catheter.

Case 3. A. L., a woman aged 40, with a diagnosis of fibroid uterus, had a subtotal hysterectomy performed. During the first 24 hours following surgery, the patient complained of severe pain in her left flank, abdominal distention, nausea and vomiting. Excretory urograms demonstrated a functionless left kidney. An attempted left ureteral catheterization disclosed an obstruction in the left pelvic ureter without extravasation. The abdomen was reopened on the third postoperative day and the ureter explored. An acute angulation of the duct was demonstrated and relieved. Apparently the condition was produced by pulling down the peritoneum to peritonealize the pelvic floor (fig. 3).

Just as surgical injuries to the ureters and bladder have increased because of the more general use of total hysterectomy, so have irradiation injuries increased because of the widespread use of radium and x-ray in the treatment of uterine malignancy, especially of the cervix. It is always advisable, before irradiation for cervical carcinoma, to perform a cystoscopic examination, including bilateral ureteral catheterization and urograms. It is only by such investigation that one can tell whether the subsequent ureteral or vesical injury is due to the operation, malignancy, or irradiation. It must be kept in mind that the most common cause of death in cervical cancer is uremia due to compression of the ureters by the malignancy.

Irradiation cystitis does not present a characteristic picture. It may be confused with chronic interstitial cystitis. Usually there is a general hyperemia and at times ulceration of the bladder wall. Occasionally the ulcers are covered with encrusted urinary salts. The most common site of the lesion is in the base of the bladder near the cervix. Biopsies always should be taken of these areas to eliminate the possibility of carcinoma of the bladder. Perhaps one of the most distressing complications following irradiation of the cervix is the development of urinary fistulas. They may open directly into the vagina or may open into the cervix and thence reach the vagina. The diagnosis is established by careful bimanual palpation of the pelvis, biopsies from bladder and cervix, cystograms, and cystoscopic study.

SUMMARY

Urologists, gynecologists, and general surgeons, all assent to the belief that the incidence of bladder and ureteral injuries is higher than available data indicate. Many clinicians are averse to reporting these injuries thereby precluding accurate statistical records, although the injuries resulting from external violence are always reported when recognized.

Ureteral injuries, particularly unilateral lesions, occurring during pelvic surgery, may not be recognized or even suspected, as the kidney may silently atrophy without giving rise to symptoms. Occasionally recanalization takes place due to the recuperative powers of these organs; however, it usually results in stricture formation. Some patients may go months or even years before symptoms develop.

Trauma to the bladder or ureter, when recognized, should always be repaired at the time of surgery. When acute symptoms develop postoperatively, suggesting ureteral injury, the employment of intravenous pyelograms, cystoscopy and ureteral catheterization will always aid in making the diagnosis, demonstrating the locations and often the extent of injury to the ureter.

When bladder symptoms or signs of fistula or ureteral obstruction develop after pelvic irradiation for malignant growths, the diagnosis is established by bimanual palpation of pelvis, cystoscopy, cystograms, and cervical and bladder biopsies.

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

THE TREATMENT OF UROLOGIC COMPLICATIONS IN GYNECOLOGY

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Injury to the ureters or bladder during performance of pelvic operations may occur in the hands of even the best surgeons. The incidence of such injuries varies from 2 per cent during performance of ordinary surgical procedures to 10 per cent during more radical operations for malignant lesions. Because of the individual variation of certain primary factors, management of injuries to the urinary tract must be highly individualized. The age and general condition of the patient, the functional capacity of both kidneys, the curability of the primary surgical lesion, and even the economic status of the patient must be weighed in conjunction with definite knowledge as to the site and type of injury.

URETERAL INJURIES

The three most common types of injury to the ureters are ligation, crushing with a hemostat, and incision or section during sharp dissection. Extensive stripping of the ureter with subsequent slough has been a less common injury. The importance of recognizing that injury has occurred before the operation is completed needs no emphasis. How often this will happen depends upon the alertness of the surgeon to its possible occurrence.

If the surgeon recognizes that he has ligated the ureter while the abdomen is still open, immediate removal of the ligature will leave little possibility for the development of fistula, but stricture may subsequently occur. In such cases, the area that has been held in the grasp of the ligature should be carefully inspected and if it is apparent that the tissue has been crushed, the area should be resected and end-to-end anastomosis performed, or the proximal end of the ureter should be implanted into the bladder, if the injury is low enough to permit this procedure.

Crushing of the ureter with a clamp usually causes enough destruction of tissue to produce permanent damage and, for this reason, the injured area should be resected and end-to-end anastomosis accomplished, or the proximal end reimplanted into the bladder.

A ureter that has been completely sectioned should be treated in the same manner. Incomplete section of the ureter may be treated by simple closure of the incised area with fine catgut sutures. It is advisable to leave an indwelling splinting catheter in place for eight to ten days, and extraperitoneal drainage should be provided in all cases.

MANAGEMENT OF LATE INJURIES

Injury to the ureter is frequently not suspected before the operation is completed. Significant diagnostic signs in the postoperative period depend upon the nature and extent of the damage. Reduced urinary excretion or complete sup-

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Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23-25, 1955.

pression of urine may temporarily follow any extensive surgical procedure, in which the blood pressure is significantly lowered However, prolonged reduction of urinary output, in the absence of shock, should never be ascribed to reflex suppression It is imperative to rule out mechanical obstruction, which can be easily accomplished by cystoscopy and retrograde catheterization In the case of ligated ureters, occasionally the catheters may be manipulated past the ligature and advanced to the kidneys, in which case they should be left indwelling until the effects of back pressure have subsided In any case, cystoscopy will establish the location of the injury Intravenous urography is also of value, and there appear to be no contraindications to it If the ureter has been severed, the function of the kidney will usually remain good and the ureter will be outlined down to the point of injury If the ureter has been ligated, the function of the kidney will be reduced in proportion to the completeness and duration of the obstruction

Ligatures probably should not be removed in the early postoperative period The local tissue reaction makes this procedure both difficult and unsatisfactory The urinary stream should be diverted by ureterostomy, pyelostomy, or nephrostomy Nephrostomy has been the most satisfactory procedure in our experience It can be performed by exposing the pelvis and lower pole of the kidney, without freeing or delivering the kidney from its bed If both ureters have been obstructed, bilateral nephrostomy can be carried out in the majority of cases, without undue risk The patient may then be allowed to convalesce in safety until the effects of back pressure upon the kidneys have completely disappeared and the tissue reaction in the area of injury has sufficiently subsided to permit performance of definitive treatment Occasionally, the ligature will absorb and the kidney will regain its normal function In the majority of cases, however, this fortunate circumstance will not occur In gynecologic procedures, the obstruction is usually low enough to reimplant the proximal end of the ureter into the bladder This will be found to be a more satisfactory solution to injuries in this area If more than two weeks have elapsed before the injury is detected, the chances of the kidney regaining its function are diminished Cases of normal renal function following obstruction, which had existed for a longer period, have been reported but one might suspect that in such cases the obstruction was not complete

In patients with irreversible renal damage, the advisability of surgical intervention must be considered If asymptomatic, hydronephrotic atrophy has occurred, the kidney may be left alone, but such kidneys if infected will require nephrectomy In the case of ureteral fistula without irreversible renal damage, the type of possible repair will be determined by the site of injury If there is sufficient length of ureter above the injury, reimplantation of the ureter into the bladder as near the normal site as possible is the procedure of choice We have, on occasion, been able to reimplant the ureter through the normal orifice That there must be absolutely no tension upon the ureter needs no emphasis The methods by which this may be done are adequately described in the literature Our experience indicates that equally good results can be obtained by each method, provided freedom from tension, constriction, and angulation is obtained

The use of a sleeve or tube constructed from the vesical wall to envelop a short ureter, otherwise incapable of reimplantation, as advocated by Ockerblad and others, may be considered. Ureteral reflux, which may follow this procedure, however, will lead to progressive renal damage. If the damaged section is short and injury too high to permit reimplantation, resection of the injured portion and anastomosis are indicated. Equally good results may be obtained from each of the several methods by which this may be accomplished. With an indwelling plastic catheter used as a splint, the lower end is drawn out through the urethra by cystoscopy at the conclusion of the operation. Alternatives are the use of a splinting catheter and diversion of the urinary stream by ureterostomy above the site of anastomosis, or splinting with a T-tube. These two methods have the disadvantage of producing angulation of the ureter, and the T-tube has a tendency to produce stricture at both ends of the T. Healing should be complete by the end of two weeks. Interval evaluation, by means of intravenous urograms and cystoscopic ureteral dilatation, is required because of the tendency to formation of stricture at the site of anastomosis.

If the damage is too high to permit reimplantation into the bladder and too extensive to permit reanastomosis, the condition of the opposite kidney will largely determine the course to be followed. If the opposite kidney is normal, nephrectomy may be a wise choice. There are those who advocate ureterointestinal anastomosis in unilateral injury, but the possible immediate and late complications cannot be considered lightly. If the kidney in question is solitary or its mate diseased, one may choose ureterointestinal anastomosis, nephrostomy, or ureterocutaneous transplantation. To await spontaneous closure of fistulas is to indulge in wishful thinking at the expense of continued renal damage. On the same basis, one should never await absorption of a ligature without diverting the urinary stream by nephrostomy to protect the kidney. Even if irreversible renal damage does not result from back pressure, the local destruction of tissue produced by the ligature will result in stricture, and in some cases, permanent occlusion of the ureter. Transuretero-ureterostomy has been advocated and unquestionably there are indications for it. In the majority of cases, however, it would seem injudicious to jeopardize the opposite normal ureter in effecting union that might result in cicatricial changes in both.

The radical treatment of malignant disease in the pelvic area not infrequently involves stripping of the ureter. In such cases, the blood supply may be compromised to the extent that the ureter will subsequently slough. This usually occurs between the end of the first and third postoperative weeks. We have noticed a considerable increase in this type of injury on surgical services, where large numbers of radical procedures are performed for pelvic carcinoma. In the cases that we have seen, the ureteral damage has been too extensive to permit resection of the devitalized area with anastomosis or reimplantation into the bladder. If the injury is bilateral, and a sufficient length of viable ureter is available, ureterointestinal anastomosis may be performed. Otherwise, the choice between cutaneous ureterostomy and permanent nephrostomy must be made. There are advocates of both methods. Our experience has been that if the stump of the ureter is brought out well beyond the cutaneous margin, there is little tendency to formation of stricture and a collecting apparatus can be worn without the aid of indwelling catheters On the other hand, if the end of the ureter should slough and retract beneath the cutaneous margin, formation of stricture is inevitable and, in such cases, nephrostomy is preferable

Obviously, individual problems will determine somewhat the course that may be followed The current practice of making preoperative intravenous urograms provides information regarding the status of renal function, which is invaluable to the operator in dealing with a ureteral injury that is recognized during the operative procedure Ligation of an injured ureter with the expectation that the kidney will undergo silent, hydronephrotic atrophy should not be considered lightly Even with the knowledge at hand that the opposite kidney is normal, if the involved kidney harbors low-grade infection, a fulminating course may be expected to follow We saw a recent case in which the back pressure following ligation of the ureter led to cortical infection and septicemia The ligature also cut through the ureter, permitting extravasation of urine through the stump Recovery followed nephrectomy and drainage of the extravasated area Ureters, in which the lumen has become constricted in the postoperative period from scar tissue, following gynecologic operation, usually lend themselves well to reimplantation into the bladder Ureterovaginal fistulas occur chiefly during vaginal operative procedures, and a case will rarely be encountered that will not lend itself to reimplantation In dealing with all types of ureteral injuries, the importance of implanting the ureter into the bladder, whenever feasible, needs no emphasis Co-operation between the surgeon and the urologist will facilitate the management of all types of ureteral injuries

INJURIES TO THE BLADDER

Injuries to the bladder will occur during performance of both vaginal and supravaginal procedures An incision into the bladder, recognized during the operative procedure, is treated by simple closure, followed by insertion of an indwelling urethral catheter Leakage of urine through the wound following supravaginal procedures is usually the result of a wound in a mobile area of the bladder, and such wounds will usually close simply by indwelling urethral catheter drainage Vesicovaginal fistulas will require plastic repair Most of these can be successfully repaired through the vagina An abdominal approach, with separation of the bladder from the vagina in dealing with high fistulas, and transvesical repair, in our experience have been less satisfactory A vesicoureterovaginal fistula will occasionally be encountered In such cases, the ureter should be cut and reimplanted into the bladder, and transvesical closure of the vesicovaginal fistula carried out at the same time or an individual problem may indicate a vaginal approach to the latter

INJURIES FROM RADIATION

The extensive application of radiation in the management of pelvic malignancies has accounted for a considerable number of urinary tract complications

The reported incidence is far below actual occurrences. The reactions in the bladder are of two types: first, acute reactions, which occur during therapy, are similar to those observed in the skin, and subside without treatment—and secondly, delayed reactions, which may appear one to eight or ten years later. These involve chiefly the lower posterior wall and floor of the bladder. The tissue change is that of endarteritis, which may lead to necrosis. About 75 per cent of these will eventually heal. In others, encrusted ulcers, vesicovaginal fistulas, or embarrassment to the upper urinary tract from obstruction of the intramural portions of the ureters, develop as a part of the sclerotic process. The majority of radiation ulcers will eventually heal and, in those cases, the bladder capacity may be restored to normal. In others, contracture will reduce the bladder capacity to the point that frequency amounts to total incontinence of urine. In such cases, the upper urinary tract is dilated. Vesicovaginal fistulas resulting from radiation reaction are impossible to repair because of the poor circulation to adjacent tissue. In both of these conditions, diversion of the urinary stream is indicated by ureterosigmoid anastomosis, if feasible. Otherwise, cutaneous transplant or nephrostomy should be done. Injuries to the urinary tract that result from radiation therapy emphasize the importance of evaluating the urinary tract in connection with the interval postoperative studies.

SUMMARY

The incidence of urologic injuries during gynecologic operations ranges from 2 per cent to 10 per cent. The method of handling such injuries will depend upon the site and type of injury, the age and general condition of the patient, the functional capacity of both kidneys, the curability of the primary surgical lesion, and even the economic status of the patient.

The most common ureteral injuries are ligation, crushing, section, and extensive stripping of the ureter. Recognition of such injuries during the operative procedure will, of course, minimize the possibility of permanent damage. Unfortunately, most of these injuries are not detected until later in the postoperative period. The importance of co-operation between the surgeon and the urologist in the management of all types of ureteral injuries cannot be too strongly emphasized.

Other urologic complications in gynecology include injuries to the bladder and those resulting from radiation treatment. Whatever the type of injury to the urinary tract during gynecologic procedures, the primary object in management is to preserve renal tissue whenever possible and to restore comfort and health to the patient.

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The Journal of Urology
Vol. 75, No. 3, March 1956
Printed in U.S.A.

IS CYSTITIS CYSTICA AN INNOCENT OR A MALEFIC LESION?

REED M. NESBIT

The discovery of small cysts in the urinary bladder is a commonplace occurrence. Most urologists ascribe their presence to low grade infection and rarely treat the lesions specifically in the belief that they are themselves harmless and will disappear when the infection has been eliminated. In fact, they are rarely biopsied. Of course, all urologists are familiar with the reports of Stirling and Ash,[1] [2] of Frank Patch[3] and others concerning the occasional occurrence of cancer in connection with cystitis glandularis, and perform biopsy in any case where there is any reason for suspicion.

The present report is made to point out that cystic lesions which are entirely innocent in appearance may in fact be composed of neoplasm and to urge that all such lesions be biopsied. The cystic lesions in question often have the appearance of small vesicles containing clear fluid while some have a yellowish or orange color and when punctured are found to contain rather thick xanthochromic material. They are rarely large, usually having a diameter less than 1 mm., and most of them are even smaller.

Most pathologists today accept the theory of von Brunn[4] that these lesions are the end product of metaplasia occurring in the transitional uroepithelium which starts as cell nests or epithelial buds. He believed that this proliferation of the epithelium was stimulated by inflammation and that the cyst formation was due to degeneration of the central cells of the nests. Today it is generally agreed that cell nests of Brunn develop as a result of chronic irritation, usually infection, but some investigations have suggested the possibility that toxins or other irritating chemical agents might provoke this type of proliferative change.

Whatever the cause, the lesions are generally seen in patients who complain of chronic, low grade bladder irritation, and infection is usually present in the urine. The experienced urologist who performs cystoscopy on such a patient will ordinarily find nothing to suggest that the cysts are anything but an objective manifestation of chronic infection and will perhaps be relieved not to have found anything of a more serious nature to treat. Of course, if ulceration of the mucosa is also present, he will be alerted to the possibility of concurrent neoplasm and will biopsy any such areas that arouse his suspicions.

The present report is concerned with a case in which typical cystitis cystica was observed in a patient who was examined by cystoscopy for low grade chronic infection. The curiosity of a urological resident physician rather than any sus-

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Read at annual meeting, American Association of Genito Urinary Surgeons, Pebble Beach, Calif., May 23–25, 1955.

[1] Stirling, W. C.: Cystitis follicularis, with discussion of other proliferative lesions of the bladder. J. A. M. A., **112**: 1326, 1939.

[2] Stirling, W. C. and Ash, J. E.: Pyelitis, ureteritis, and cystitis cystica, follicularis, glandularis and granulosa with a note on their pathogenesis. J. Urol., **45**: 381, 1941.

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[4] von Brunn, A.: Über Drusenahnliche Bildungen in der Schleimhaut des Nierenbeckens des Ureters und der Harnblase beim Menschen. Arch. f. Mikr. Anat., **41**: 303, 1893.

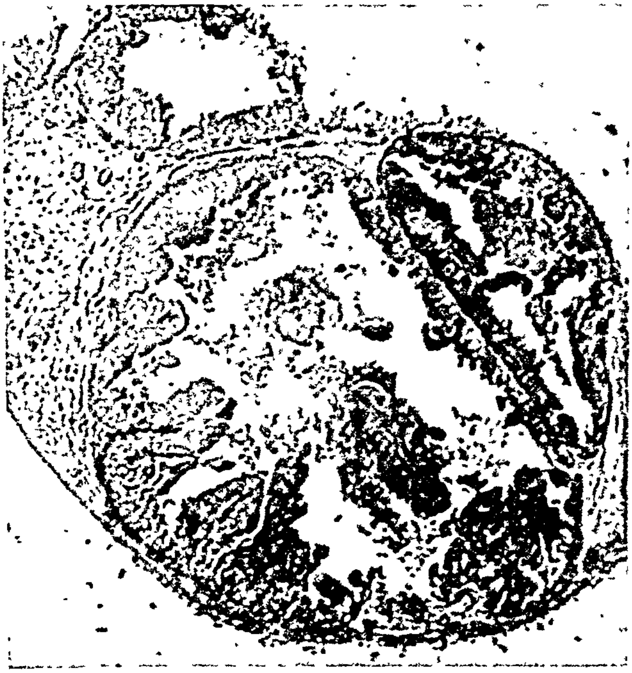

FIG. 1. Cyst removed at first biopsy. Low power. This demonstrates papillary neoplasms which are not invasive.

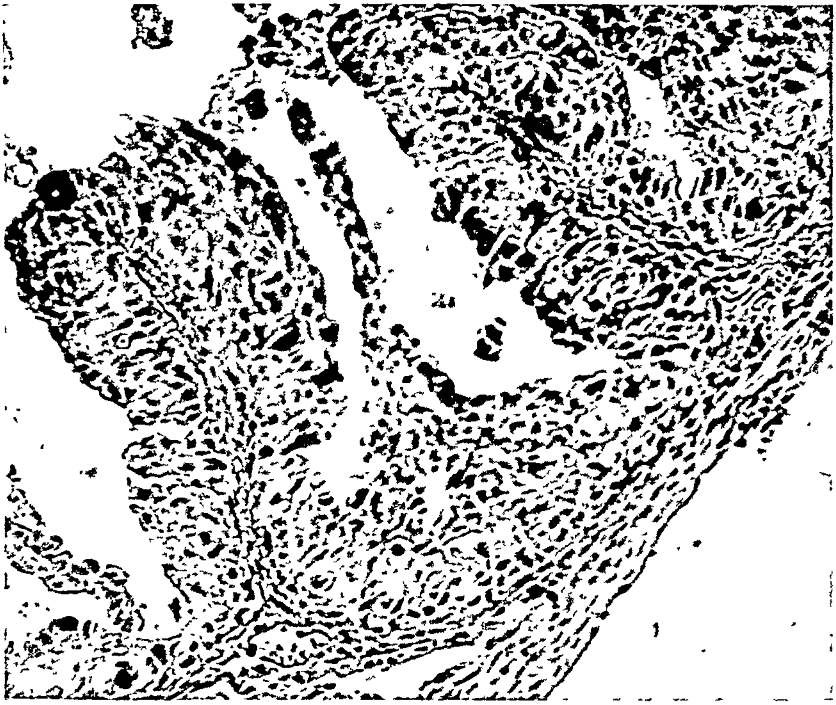

FIG. 2. High power of cyst removed at first biopsy

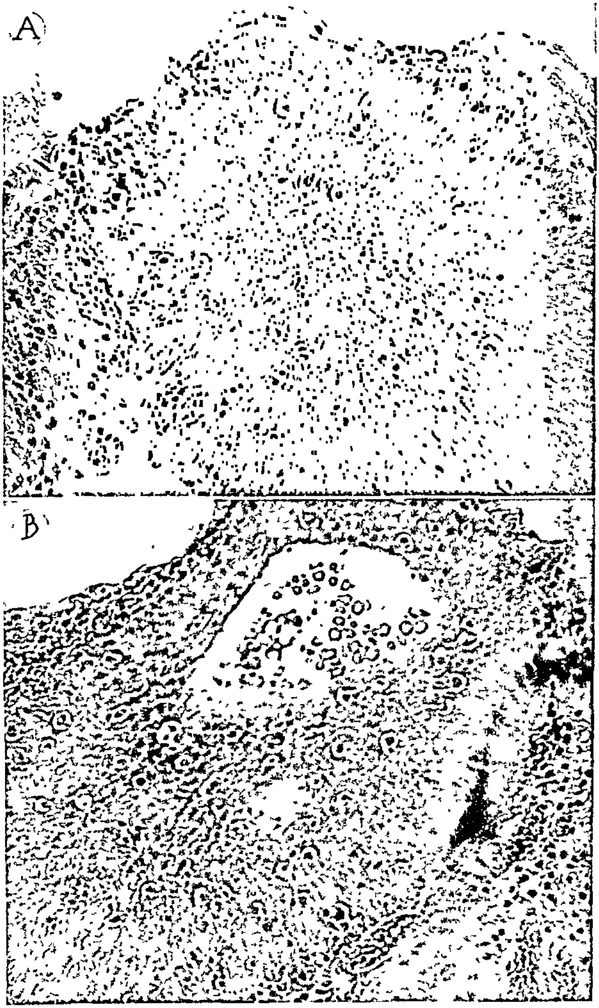

FIG 3 A, typical cell nest of Brunn. Tissue removed at second biopsy. *B*, degenerating cell nest of Brunn; typical lesion of cystitis cystica.

picion of cancer led to the performance of biopsy and neoplastic disease was found.

The patient, U.M. No. 797504, was a 49-year-old Mexican laborer who complained of irritative bladder symptoms present for 5 months. These symptoms had become progressively worse, and at the time of admission he was incapacitated because of great pain on urination and voided every 15–30 minutes by day and seven to eight times at night. The urine contained only an occasional red blood cell and no white cells, and the stained sediment revealed numerous gram-positive cocci. The prostate gland was not enlarged.

Dr. James Morrow, first year resident on our urological service, performed a cystoscopy and found diffusely spread pustules throughout the bladder, but especially in the trigonal area. The intervening bladder did not appear especially abnormal. He was informed by his preceptor, who also looked into the bladder, that these were typical lesions of cystitis cystica, but in his inexperience he decided to find out how such a lesion would look under a microscope. He removed one of the cysts with a biopsy forceps, then went on with the completion of his retrograde study of the patient.

The microscopic sections reveal that the entire cyst was removed without distortion and that it contains several small papillary neoplasms which are not invasive (figs. 1 and 2). A few days later the patient was examined by cystoscopy,

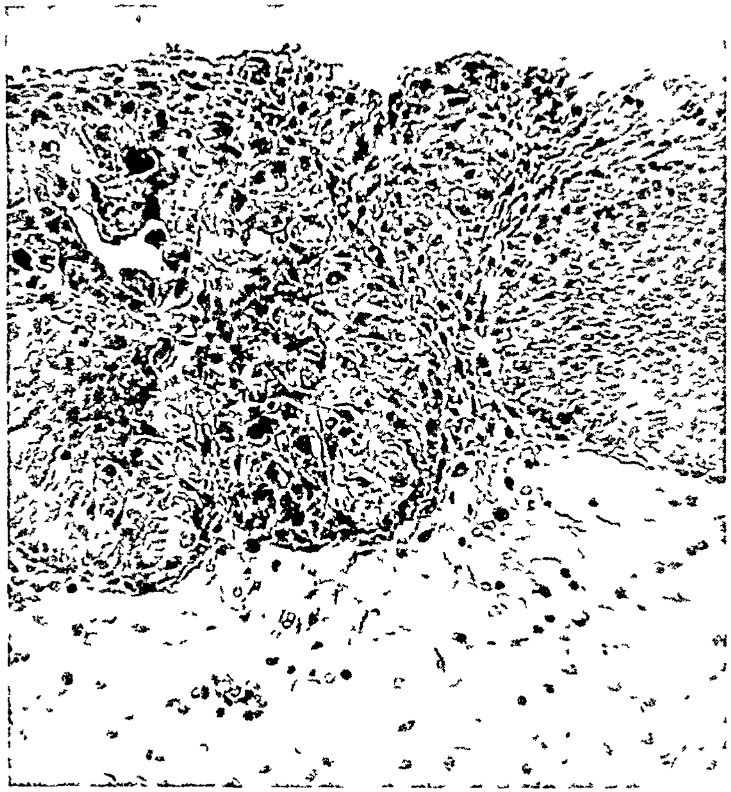

FIG 4 Area of intramucosal carcinoma "carcinoma in situ"

and again the bladder was observed to have several typical lesions of cystitis cystica on and about the trigone Again it was observed that there were no areas that in any way had the appearance of neoplasm Further biopsy specimens of larger size were removed with the Lowsley cystoscopic rongeur These specimens revealed a variety of lesions some were typical cell nests of Brunn (fig 3, *A*), some were typical of cystitis cystica (fig 3, *B*), but there were several cysts in which neoplasm was present Also, there were areas of the surface bladder mucosa which showed intramucosal carcinoma of the type generally termed "carcinoma in situ" (fig 4) The involvement was so extensive on the bladder floor that it was felt that no treatment short of total removal would offer hope of cure and cystectomy was performed Further microscopic study of the bladder revealed widespread involvement

Certain features of this case have been of especial interest They have provided us cause for reflection and have given your essayist a rude awakening concerning the malefic potentialities of cystitis cystica I can well remember the time when, as a resident in urology, I first encountered lesions of this type Prompted by curiosity regarding the composition of the pustule like cysts, some of them were removed with biopsy forceps for microscopic examination Some of them simply burst and exuded their liquid contents while others, more solid in character, proved to be cell nests like the lesions described by von Brunn Since that early experience I must confess that I have never removed any more of the cysts for biopsy To be sure, many cases which displayed this phenomenon have been biopsied when contiguous areas of the mucosa have appeared to be suspect and cancer has been observed in their vicinity on several occasions

In the present case the enquiring resident surgeon had no reason to suspect neoplasm, and he removed only one lesion—a pustule like cyst which he chose at random from several Other, similar appearing lesions removed later from the same area were the typical cell nests of Brunn—some solid, some cystic—so the chance selection of a neoplastic cyst was entirely fortuitous Had he picked one or more of the nonneoplastic cysts at the time of the first biopsy, cancer would not have been diagnosed or even suspected

Another feature of the case which provides some cause for speculation is the finding of papillomas wholly within several of the cysts This suggests the possibility that the factor which initiated proliferative changes in the epithelium was not infection, as appears usually to be the case when cysts occur, but perhaps a chemical carcinogenic agent Several investigators[5] [6] of these lesions in the past have suggested that toxins or other irritating nonbacterial constituents of the urine might provoke the formation of cell nests of von Brunn

Certainly this unusual case has caused us to revise our attitude toward the lesions which we call cystitis cystica It is our plan to take biopsies of several of the lesions whenever found, for they cannot be considered innocent until proven so

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[5] Giani R Experimenteller Beitrag zur Entstehung der Cystitis Cystica Centralbl f Allg Path u Path Anat 17 180 1906 Ibid p 900

[6] Herxheimer G Uber Cystenbildungen der Niere und Abfuhrenden Harnwege Arch f Path Anat 185 52 1906

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

EXSTROPHY OF THE URINARY BLADDER: ITS TREATMENT BY PLASTIC SURGERY

THEODORE H. SWEETSER, TAGUE C. CHISHOLM, WILLIS H. THOMPSON, ELDON B. BERGLUND, STANLEY P. WESOLOWSKI AND T. H. SWEETSER, JR.

This presentation is a report of progress in the management of 12 cases of exstrophy of the urinary bladder during the past 6 years. We are convinced that plastic reconstruction of the exstrophied bladder and abdominal wall with urinary control is based on sound surgical principles and should be consistently successful. We have tried to make the procedure as logical and simple as possible with a resulting urinary tract as close to the normal as possible.* We hope that more widespread interest in the problem will lead to improved techniques and further demonstration of practicability.

We are among many workers who share dissatisfaction with the conventional ureterosigmoidal transplantation for the relief of patients with exstrophy. Simultaneously we are encouraged by the small but increasing number of urologists who recognize that plastic reconstruction of the exstrophied bladder and abdominal wall with urinary control is feasible.

Based upon our experience with 10 cases since our original report in 1952,[1] we are more confident than originally that plastic surgery can consistently produce a satisfactory bladder and urethra with good sphincter control. At the same time we appreciate more than we did in 1952 many of the technical challenges and the not-so-simple solutions.

There are three principal objectives: 1) satisfactory closure of the bladder, 2) closure of the abdominal wall, and 3) provision of adequate voluntary urinary control.

BLADDER RECONSTRUCTION

Our method of replacement of the bladder and displacing the peritoneum from behind is illustrated by these diagrammatic sagittal sections used in our preliminary report (fig. 1).

On the whole this approach has been satisfactory for male children. In female children we have found that placing of the perineal traction suture is more difficult because of the need of going lateral to the vagina. Also in the female this suture is less valuable because the peritoneum can not be stripped from the anterior surface of the uterus above the cervix. We have found that suturing of the obliterated hypogastric arteries across in front of the bladder has held it back

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Read at annual meeting, American Urological Association, Los Angeles, May 16–19, 1955.

* Our effort receives additional support from a statement of Professor George Huntington (Columbia University College of Physicians and Surgeons) quoted by Dr. T. J. Kirwin who discussed a paper just before ours on this program; we are indebted to Dr. Kirwin for the quotation: "Any surgeon in approaching a surgical operation, regardless of which organ, should disturb the normal anatomy in the least manner possible. If this is followed out, it will be better for the patient and cause less headaches for the surgeon."

[1] Sweetser, T. H., Chisholm, T. C. and Thompson, W.: Exstrophy of the urinary bladder: Discussion of anatomic and surgical principles applicable to its repair, with preliminary report of a case. Minn. Med., **35:** 654–657, 1952.

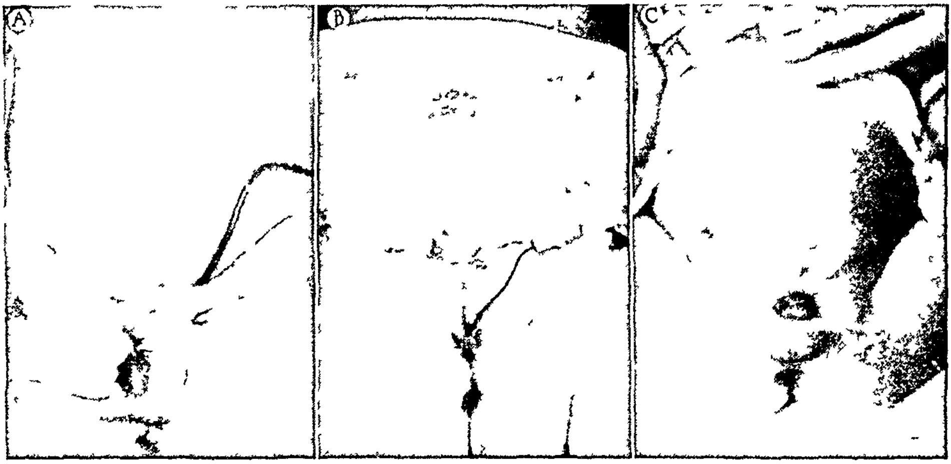

FIG. 3

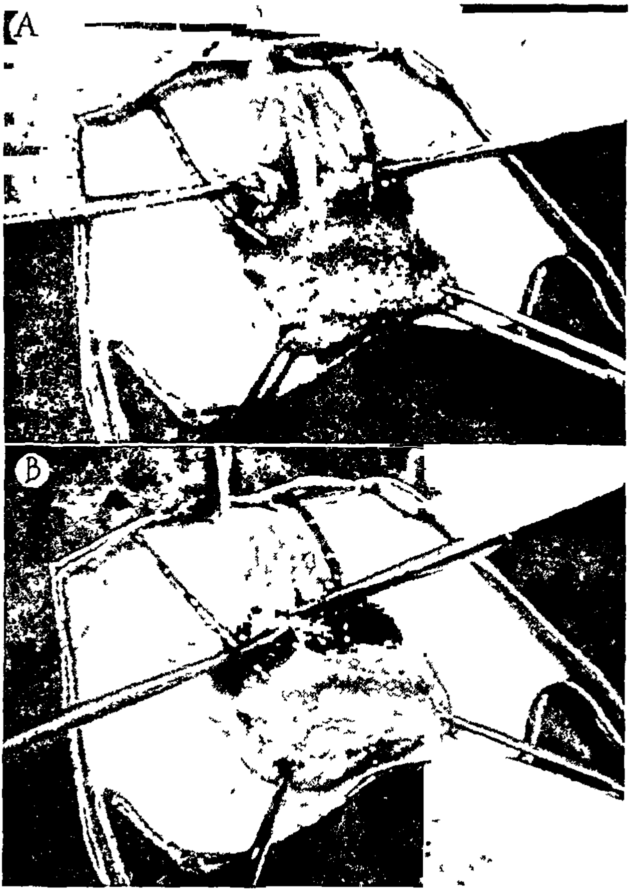

FIG. 4. Muscle for external sphincter, and its method of closure, demonstrated, in practice, urethral tube is closed before closure of sphincter

TABLE 1

Extent of Repair	Complications	Status in May 1955
	7 Boys	
1* Bladder only	Tiny bladder Complete disruption	Died after subsequent ureterosigmoidal transplant
3 Bladder Posterior urethra	Tiny bladder	Has a good bladder but no control yet Surgery not finished
8 Bladder Posterior urethra External sphincter	Cystitis cystica Neurogenic defects Bladder fistula	Surgery not finished
7 Bladder Posterior urethra External sphincter	Tiny bladder	Control unknown Surgery not finished
9. Bladder External sphincter Epispadias	Bladder and urethral fistula	Surgery not finished
2 Bladder Epispadias	Urethral fistula	Temporary control with fistula closed Surgery not finished
5 Bladder External sphincter Epispadias	Urethral fistula	Temporary control with fistula closed Surgery not finished
	5 Girls	
1 Bladder only	Bladder fistula	Some control Has refused permission for further plastic surgery
6 Bladder Urethral sphincter	None	Excellent control Good bladder capacity
10 Bladder Urethral sphincter	None	Excellent control Fair bladder capacity
11 Bladder Urethral sphincter	None	Excellent control Fair and improving bladder capacity
12 Bladder Urethral sphincter	None	Excellent control Fair and improving bladder capacity

* Case numbers indicate chronological order.

against the uterus, which with the broad ligaments thus furnishes good protection against anterior pressure by intraperitoneal viscera We feel also that such use of the obliterated hypogastrics can be of supplementary value in males by helping to keep the peritoneum out of the lateral recesses of the pelvis.

ABDOMINAL WALL RECONSTRUCTION

In all our cases closure of the abdominal wall has been accomplished. For the deep layers each anterior rectus sheath has been developed as a book flap (fig. 2),

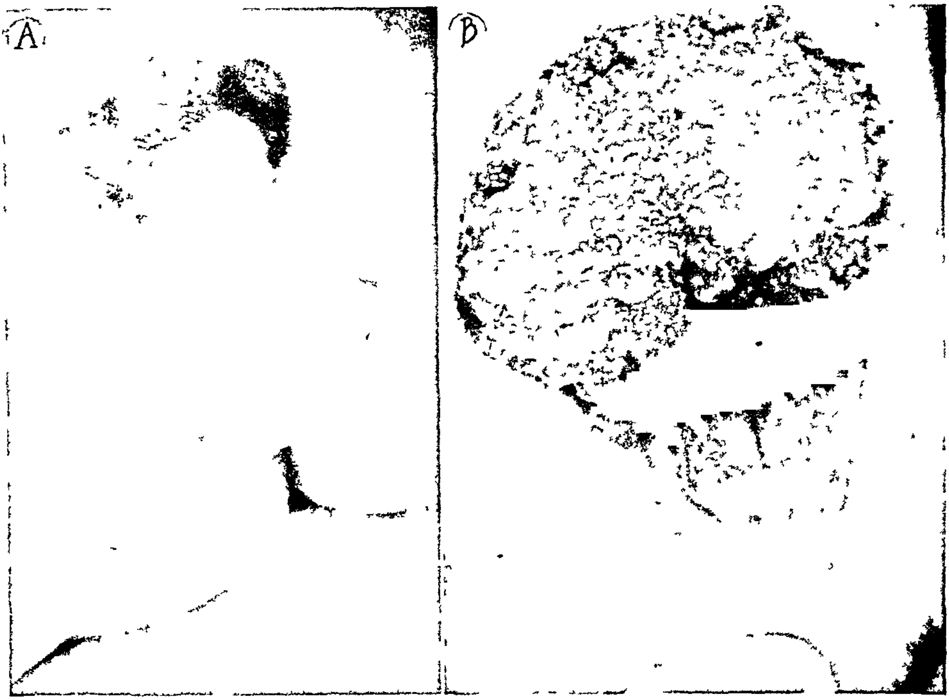

FIG. 5. *A*, Case 4. bladder. *B*, Case 8. Cystitis cystica

turned over and downward and sutured to the opposite side with interrupted silks. For the superficial layers the skin and underlying fat have been closed in several ways: by rotating and advancing flaps (fig. 3, *A*); by sliding double pedicle flap with "Y" closure (fig. 3, *B*); and by simple undermining, mobilizing and suturing in the midline (fig. 3, *C*). The simple midline suture had been easiest and most effective when feasible.

URETHRAL VOLUNTARY SPHINCTER RECONSTRUCTION

The third objective of our treatment, the adequate provision of voluntary control, is, of course, essential for success. Since first appreciating and utilizing the transverse posturethral intersymphyseal band, the incomplete triangular ligament in 1953,[2] we have found it to be present and usable as a sphincter consistently in all our male and female patients. The studies of Drs. Frank Preston and Theodore Sweetser, Jr.[3] have not yet completely answered all questions regarding its derivation but our biopsies have repeatedly shown the presence of striated muscle. In all but the first patient we have separated both ends at the symphyseal attachments, avoiding injury of the nerves and vessels (fig. 4, *A*), and have overlapped them in front of the newly closed urethra (fig. 4, *B*). After using this tissue bundle in our last 6 cases, we see no reason to question its availability and effectiveness as a voluntary sphincter.

[2] Sweetser, T. H.: Exstrophy of the urinary bladder; further study of treatment by plastic surgery. A.M.A. Arch. Surg., **68:** 525–530, 1954.

[3] Preston, F. S. and Sweetser, T. H., Jr.: Personal communication.

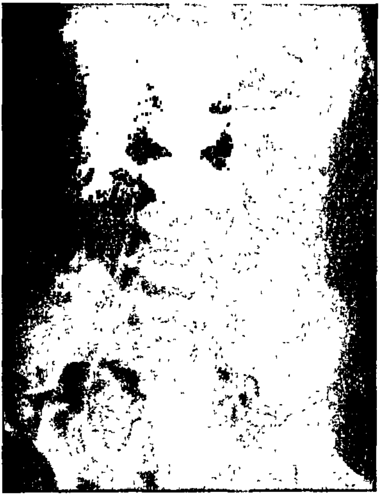

Fig. 6. Case 8. Preoperative excretory urogram

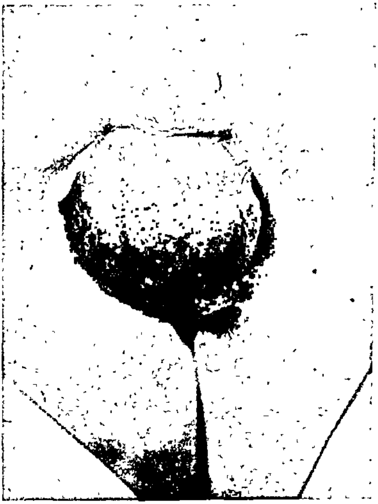

Fig. 7. Case 10. Umbilical hernia

DIFFICULTIES AND COMPLICATIONS

These have plagued us (table 1); we should like to mention a few. 1) Various other associated congenital anomalies have influenced the treatment, such as the small, inelastic bladder (fig. 5, *A*), cystitis cystica (fig. 5, *B*), congenital unobstructed hydroureter and hydronephrosis (fig. 6) and other neurogenic defects, reduplications in the upper urinary tract, prolapse of the rectum, congenital inguinal and umbilical hernias (fig. 7), subluxation of the hips and deformities of the spine. 2) Infection is often present at the start, and may be a stubborn and disheartening problem in spite of antibiotics and careful attention to basic surgical principles. 3) Prevention of ureteral reflux by a modified Hutch ureteroplasty has been fairly successful but we are not yet satisfied that it is always necessary. Perhaps it should be done later as a separate procedure when needed. 4) The blood vessels supplying the bladder are closer to the anterior abdominal wall laterally than we expected and should be avoided in freeing the bladder. We came close to disaster in one case while mobilizing the bladder wall. 5) We have previously made some suggestions regarding patients with tiny, inelastic bladders. The suggestions of Folsom[4] and Richardson[5] may still be applicable. We found in one case that use of the vesical mucosa as a framework for bladder reconstruction after stripping off the fibromuscular layers was not very successful, probably because of inadequate blood supply. We are eagerly watching progress of the work of Shoemaker and associates[6, 7] for its possible application to this problem. 6) Closure of the urethra and bladder should be done with interrupted sutures of fine chromic catgut, not with continuous suture. 7) The cystostomy tube which has given us best results thus far, after trying various types and materials, has been a rubber two-wing Malecot catheter of adequate size. In some cases we have treated it with silver nitrate solution as advised by Ockerblad.[8] 8) Until recently we have left a nylon guide thread through the urethra (somewhat as used by Young,[9] but in the last 2 cases, after hearing and reading of Frank Hamm's experiences,[10] we have left nothing in the urethra; we hope that time will prove us correct. 9) Careful attention to fluids and electrolytes immediately before and after operation helps to avoid trouble. Too much fluid gives as much trouble as too little. 10) Several patients had mild convulsions after surgery, which, while not fully explained, were controlled well by giving intravenous magnesium sulphate solution. 11) Extreme hypertension occurred in one case, twice, soon after surgery; pressure returned to normal without mishap when hexamethorium bromide was given 12) Two of our male patients have had a persistent very small fistula ventrally at the base of the penis Other workers[11] have reported similar difficulty in treating the epispadias

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[4] Folsom, A. I., O'Brien, H. A. and Caldwell, G. T.: Subtotal cystectomy in the treatment of Hunner's ulcer. J. Urol., **44:** 650–666, 1940.

[5] Richardson, E. J.: Bladder regeneration. Minn. Med., **35:** 547–549, 1952.

[6] Shoemaker, W. C. and Marucci, H. D.: Experimental use of seromuscular grafts in bladder reconstruction. J. Urol., **73:** 314, 1955.

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[8] Ockerblad, N. F.: Reimplantation of ureter into bladder by flap method. J. Urol., **57:** 845–847, 1947.

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[10] Hamm, F. C. and Weinberg, S. R.: Renal and ureteral surgery without intubation. J. Urol., **73:** 475, 1955.

Much remains to be done, and we will be happy to hear of the experiences and improved techniques of any who will join in meeting this challenge

At present we believe that exstrophy of the urinary bladder can be successfully treated by plastic surgery, with consistently successful construction of an adequate bladder and urethra closely simulating the normal, and with provision of good urinary control

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[11] Dees, J E Congenital epispadias with incontinence J Urol , 62 513, 1949

The Journal of Urology
Vol. 75, No. 3, March 1956
Printed in U.S.A.

PARTIAL CYSTECTOMY FOR THE HYPOTONIC BLADDER: REPORT OF ELEVEN CASES

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Normal micturition involves four factors: expulsive force, opening of the internal meatus by the trigone, an external sphincter capable of relaxing, and a patent urethra. Normal expulsive force implies a normally innervated detrusor which responds to critical filling by complete emptying. Since diagnosis and treatment of mechanical obstruction to urination yield satisfactory results, urethral patency will not be discussed. By contrast the recognition, and particularly the correction, of reduced expulsive force may be difficult or impossible.

Four types of disorders weaken the detrusor. The first, neurogenic vesical dysfunction, may be central or peripheral, sensory or motor. Excluding trauma, the commonest variety probably results from an incomplete destruction or congenital deficiency of cells or fibers for vesical sensation in the spinal cord, peripheral nerves, or vesical plexus. Impaired sensation leads to chronic vesical distension which so interferes with venous return as to render the detrusor hypoxic. This causes hypotonia and later atrophy of the detrusor, i.e., impaired expulsive force. Included in this group is the hypotonic bladder sometimes associated with megaloureters. Swenson et al. attribute this to scarcity of ganglia in the vesical plexus; Powell calls it "megalobladder."

The second is neglected mechanical obstruction, exerting the same effect upon the detrusor as sensory neurogenic dysfunction. Relief of obstruction is curative unless advanced atrophy prevents effective contraction. Hermann, and Crabtree and Muellner have attributed this to a patchy replacement of detrusor fibers by fibrous tissue.

Third, excision of the rectum may, according to Campbell, cause sufficient pericystitis with edema of the detrusor to impair expulsion of the urine.

Last is reduced expulsive force of unknown origin, usually called "atonic bladder." Since such bladders do exhibit reduced rather than absent expulsive force, the term "hypotonia" is more accurate. In 1908 Shattock likened it to idiopathic dilatation of the esophagus, stomach, and colon. A year later Asch, reporting 11 cases, suggested disease of the vesical nerves or ganglia as a cause, while Thomson-Walker spoke of a lesion of a "sympathetic reflex center" in the hypogastric and hemorrhoidal plexuses. Geraghty (1917) suspected a peripheral neuritis. Kretschmer and Heckel reviewed the whole subject in 1932. Houtappel has recently postulated a defect in the detrusor fibers themselves.

Commoner in the female, primary hypotonia causes increased frequency and difficulty of urination with considerable residual urine without complete retention; it probably begins with unnoticed, infrequent micturition. Psychiatric and neurological disorders and mechanical obstruction are absent. Capacity is large,

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Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23-25, 1955.

expulsive force is reduced, trabeculation is minimal or absent, and there are no diverticula large enough to contain the residual urine Sensation is intact A complicating cystitis may overshadow the underlying cause The upper tract is normal, since intravesical pressure is low Diagnosis is made by exclusion

TREATMENT OF PRIMARY HYPOTONIA

While residual urine is still small, complete emptying may be achieved with cholinergic drugs, urination at regular intervals in two or more stages, and manual suprapubic pressure If this regimen fails, the internal sphincter may be weakened by transurethral resection However, these patients are rarely seen by the urologist until residual urines are large, when conservative measures, as well as transurethral resection, usually fail

Since the hypotonic bladder can expell a considerable volume, it should be possible to eliminate residual urine by reducing vesical capacity Because the vesical nerves ramify from a plexus beneath the trigone, and most of the blood vessels come from behind and laterally, one may remove the vertex with portions of the contiguous walls without damaging the remaining bladder This was apparently done first by Orr in 1937, and later by Crabtree and Muellner, by Fish, and by Houtappel Together they have reported 24 cases, mainly of neglected mechanical obstruction, with fairly uniform improvement In order to secure consistent results, I have resected enough of the dome of the bladder so that the remnant can be sutured snugly about a Kearns balloon inflated to 300 cc and subsequently withdrawn, wedge excision of the posterior lip of the vesical orifice with transverse suture is usually done as well Cystostomy is maintained for two weeks thereafter

CASE REPORTS

Case 1 Mrs K B, aged 32, University Hospital No 850716, had always urinated frequently, and was told in 1947 that she had a large residual urine, although no treatment was suggested Once, after removal of 2 liters of residual urine, she did not urinate for 36 hours Retrograde pyelograms in August 1952 were normal and a cystogram showed a large, nontrabeculated bladder She had had 2 cesarian sections

In September 1952, residual urine measured 1500 cc, and capacity was 2000 cc The urethra, ureteral orifices, and bladder were otherwise normal except for poor expulsive force Neurological and serological examinations yielded normal results

At operation on October 30, 1952, the internal urinary meatus felt normal and the bladder was normal except for its size Partial cystectomy was done, and she was discharged 16 days later without residual urine

She had no complaints whatever referable to her bladder until March 1955 when, following recovery from division of adhesive bands for acute intestinal obstruction, she felt that she was again retaining urine On March 22, 1955, an excretory urogram was normal but there were 785 cc residual urine An inlying catheter was inserted, but she again suffered acute intestinal obstruction, 10 days after operation she began to empty her bladder completely

Case 2 Mrs E L, aged 44, No 645918, had poliomyelitis in childhood, but difficult urination did not appear for many years. Transurethral resection and urethral dilatations then failed, and overflow incontinence appeared shortly before admission. The only positive finding on general, neurological and serological examination was slight weakness in one upper extremity. There were 450 cc clear residual urine, and the upper tract was normal. At cystoscopy the urethral aspect of the internal meatus was scarred but flexible and open. Mild cystitis was present with a capacity of 1100 cc. On January 5, 1953, plastic widening of the internal urinary meatus and partial cystectomy were done. She was discharged on the sixteenth postoperative day without residual urine.

On March 7, 1955, 26 months later, she was voiding somewhat more often than normal. The internal meatus was unchanged; there was mild cystitis with a capacity of 500 cc, and 30 cc of clear residual urine containing Bacillus proteus. This is being treated.

Case 3. Mrs. L. A., aged 44, No. 875683, had symptoms of obstruction to urination for several years. A month before admission dysuria and pyuria appeared, and her physician found residual urines ranging from 250 to 350 cc. Antibiotics relieved the irritation, but cholinergic drugs and urethral dilatations did not reduce the residual urine. The kidneys were normal.

On October 11, 1954 the urethra was normal. The bladder was large and faintly trabeculated, and expulsive force was poor. Cystogram (fig. 1) showed only a large bladder. Neurologic and serological examinations yielded normal results. At operation on October 13, 1954, the bladder was large and thin walled. The internal meatus admitted the forefinger. Therapy was like that in case 2.

FIG 1. Case 3 Cystogram of primary hypotonia

She was dismissed on the seventeenth postoperative day urinating normally without residual urine On May 4, 1955, seven months after operation, she was asymptomatic, her physician found 10 cc clear residual urine containing Escherichia coli

Case 4 Mrs V G , aged 67, No 871811, complained of urinary obstruction increasing in severity for several years She was a rather neurotic widow with essential hypertension

On admission there were 190 cc sterile residual urine Excretory urography and neurological as well as serological examination yielded normal results The urethra, ureteral orifices, and bladder were normal except for a vesical capacity of 800 cc with impaired expulsive force

Operation on June 24, 1954 was identical with that in cases 2 and 3 When the suprapubic tube was clamped on the fourteenth day, she voided normally When it was withdrawn, she was completely incontinent without residual urine Cystoscopy disclosed no cause for the incontinence Houtappel commented upon the frequency of partial incontinence in his postoperative patients She was discharged with an inlying catheter on the twenty-first postoperative day to the care of her physician Three months later he reported that the residual urine was 60 cc "an hour after voiding "

Nine months after operation she wrote that she was getting up once at night with normal diurnal frequency, long postponement occasionally caused incontinence The end result is good, but convalescence was slow and unpleasant

Here are 4 women ranging in age from 32 to 67 with large residual urines without neurological disorders or mechanical obstruction to urination Their disorder is probably best called primary hypotonia of the bladder All responded well to partial cystectomy While this was supplemented in three by plastic widening of the vesical neck, cystoscopic evidence indicated that this was unnecessary, and it was done to avoid subsequent operations if possible None of the patients has significant residual urine 7 to 27 months after operation One remained well for 30 months, then relapsed after an operation for acute intestinal obstruction This is not surprising, since the detrusor fibers of these people are probably inherently abnormal However, she subsequently recovered her ability to empty the bladder

In the presence of complete retention, one must be wary of neurological and psychiatric disorders before blaming primary hypotonia, as illustrated by case 5 Sister C S , a nun aged 27, No 871088, had difficult urination for 2 years During the month preceding admission, she had several attacks of acute retention with volumes up to 1500 cc Use of cholinergic drugs with intermittent and inlying catheterization had been futile

The residual urine on admission measured 400 cc General and serological examinations were not informative The neurological consultant suspected multiple sclerosis but could not prove it There was spina bifida occulta of the first sacral vertebra The upper urinary tract, the spinal fluid, its pressure, and a spinogram were normal The cystogram showed a large, nontrabeculated bladder

Cystoscopy disclosed no abnormality except a capacity of 900 cc with impaired expulsive force but normal sensation. Cholinergic drugs, suprapubic pressure, two-stage urination, and catheterization did not induce normal urination.

On June 10, 1954, plastic widening of the internal meatus and partial cystectomy were done. She was discharged without residual urine on the twenty-first postoperative day. Within a week the residual urine reached 500 cc. Intermittent catheterization and cholinergic drugs failed. She was readmitted on September 21; nothing abnormal was noted at cystoscopy. The neurologic findings were unchanged. Transurethral resection of the internal sphincter was done twice without benefit. Pudendal blocks with procaine were futile. Suprapubic cystostomy was re-established on October 5, 1954 and she was discharged on October 11.

On March 9, 1955 her physician reported that residual urine with the tube clamped was 250 cc, and that it fell to zero after a pudendal block with procaine. When this was repeated with saline, the result was the same.

It seems in retrospect that she has hysterical urinary retention based upon dissatisfaction with the ascetic life, and that psychiatric examination should have been made before operation was considered, but multiple sclerosis has not yet been excluded.

OTHER TYPES OF HYPOTONIA

Patients with other types of hypotonia may benefit from partial cystectomy. In *case 6*, residual urine persisted after complete removal of *mechanical obstruction*. Master D. P., aged 4, No. 784087, had always had a large abdomen, pyuria, and frequent, dribbling urination. The abdominal muscles were absent; intestinal peristalsis was visible. There were 600 cc cloudy residual urine, and urography showed a much dilated solitary left kidney and ureter (fig. 2, *A*) with a large bladder containing 2 small diverticula at the vertex (fig. 2, *B*). Cystoscopic examination disclosed a contracture of the vesical neck with a large, untrabeculated bladder having poor expulsive force.

Transurethral resection reduced the residual to 150 cc. On January 27, 1948 about one-third of the wall of the bladder, including the 2 diverticula, was

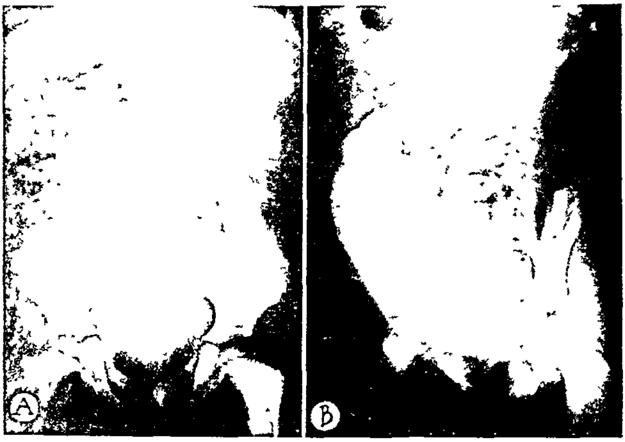

FIG. 2. Case 6. *A*, urogram in congenital absence of abdominal muscles. *B*, cystogram

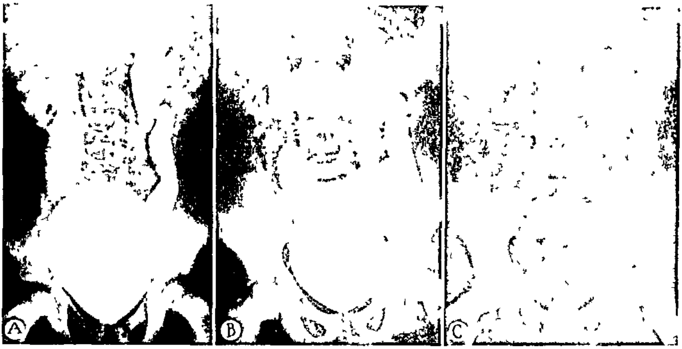

FIG. 3. Case 7. *A*, congenital megalobladder with reflux before operation *B*, cystogram in same patient 6 months after partial cystectomy *C*, after three consecutive urinations

excised, with primary closure. No abdominal muscles were found. He was discharged 2 weeks later without residual urine. His father refused to bring him back but wrote, 7¼ years after operation, that he had remained perfectly well, and enclosed a photograph of a robust boy of 11. An excretory urogram made in July 1955 through the courtesy of Dr. P. J. Steiner of Lemmon, South Dakota showed that the upper urinary tract had not changed since his original admission nearly eight years ago.

Congenital ureterectasis has been mentioned, and is illustrated by *case 7*. Master P. L., aged 6, No. 869333, had always had pyuria with bouts of chills and fever. Another cystoscopist had said that he had bilateral hydronephrosis from obstruction at the vesical neck. Upon admission 2 days later he had a temperature of 104F, a urea nitrogen of 50, and 450 cc of turbid residual urine containing Aerobacter aerogenes. With antibiotics and an inlying catheter the temperature and urea nitrogen returned to normal. Cystography then outlined a large, smooth bladder with reflux delineating grade 3 bilateral hydronephrosis with correspondingly dilated ureters (fig. 3, *A*). At cystoscopy the internal meatus gaped, the ureteral orifices were dilated, the bladder was not trabeculated, and expulsive force was poor.

After continuous suprapubic drainage for 3 months, a cystogram showed no improvement of the bladder but the upper tract had improved a trifle. At operation on June 24, 1954, the detrusor was thick and pale without evidence of contractility, and the internal meatus stood open. Wedge excision and transverse closure of the posterior lip of the internal meatus, and partial cystectomy were performed. Cystostomy was continued for a month, after which timed two-stage urination, manual suprapubic pressure, and very small doses of antibiotics were instituted.

In January 1955, the clear residual urine measured 30 cc. Cystography showed a smaller bladder with reflux (fig. 3, *B*). The upper tract was unchanged. Stephens' regimen was then tried: roentgenography after micturition showed about one-half of the contrast agent in the upper tract; a second effort removed about half of it; a third attempt almost emptied the kidneys (fig. 3, *C*). His mother was instructed to have him void 3 times with suprapubic pressure at each sitting, every three hours during the day, and once at night. He was reported well in April 1955.

Experience suggests that partial cystectomy is applicable to other types of neurogenic dysfunction only if there is sufficient sensation to permit active cooperation in emptying the bladder. *Cases 8* and *9* are pertinent. Two girls, T. M., aged 12, hospital No. 755751, and M. M., aged 8, hospital No. 755681, had overflow incontinence following operations early in life for meningomyelocele, and both had large bladders with advanced bilateral hydronephroses. Each had futile trials of cholinergic drugs, urination by the clock, suprapubic manual pressure and, finally, transurethral resection. Partial cystectomy reduced the residual urine from 200 to as low as 30 cc in T. M., but she is still incontinent. The low residual justifies procrastination; if improvement does not occur, diversion of the urine through an isolated ileal loop (Bricker) may be considered. The other patient was freed of residual urine for a brief period, only to relapse. Bricker's operation was then done because of progressive hydronephrosis.

When the patient has enough sensation to permit him to help himself, results are better, as in *case 10*. G. M., No. 655609, a man of 60, had "infantile paralysis" in childhood and had been incontinent of urine until 1935, when reduced sensation to pinprick and light touch was found below T 11, indicating that his original illness was a transverse myelitis. Transurethral resection yielded complete relief until 1952 (17 years), when small stream, hesitancy, straining, and urinary incontinence recurred.

On readmission in July, his neurologic status was unchanged. The prostatic urethra was well resected and smooth; the residual urine was 150 cc and sterile. The bladder was trabeculated and held 700 cc.

Suspecting a hypotonic detrusor from the old neurogenic lesion, trocar cystostomy was established for 3 months. The tube was then clamped, but residual urine was the same. About one-third of the bladder was removed in October 1952, and he was discharged 2 weeks later without residual urine. He reported in March 1955, 29 months after operation, that improvement had persisted, but that he still had intermittent incontinence.

Case 11. Mrs. C. F., aged 69, No. 812750, had mild neuropathy secondary to diabetes of 26 years' duration. Urinary infection had recurred and relapsed for years, and transurethral resections in 1951 were ineffective. In April 1954 she had a nontrabeculated bladder with a capacity of 1200 and a residual of 450 cc containing Aerobacter aerogenes. There was no urethral obstruction. Partial cystectomy was done. Eleven months later there were 90 cc infected residual urine, but capacity was now 550 cc, and the upper urinary tract was normal. Antibiotics had not influenced the infection.

Comment. Objective has greatly exceeded subjective improvement; the pronounced reduction in both residual urine and capacity seem worthwhile.

PATHOLOGIC FINDINGS

There were no consistent histological changes in the bladder by which the nature of the complaint could be identified There was evidence of infection in the mucosa and submucosa in most instances, but the muscularis appeared normal, even in the patient in whom it seemed pale and fibrous at operation

SUMMARY AND CONCLUSIONS

Eleven patients have had partial cystectomy to eliminate residual urine from loss of expulsive force in the absence of mechanical obstruction The capacity of the bladder was reduced to 300 cc, and cystostomy was maintained for 2 weeks In all but two, plastic widening of the internal sphincter was also done For convenience the types of lesions and results have been classified as follows

Group I Primary hypotonia
  A Psychologically and neurologically normal 4 cases, 4 cures (One patient relapsed after operation for acute intestinal obstruction 30 months after partial cystectomy)

Group II Hysterical urination retention?
  Psychoneurotic with questionable neurological findings (multiple sclerosis?) 1 case, failure

Group III Mechanical obstruction
  Psychologically and neurologically normal Residual persisting despite relief of obstruction 1 case, 1 cure

Group IV Neurogenic vesical dysfunction
  Psychologically normal, lesion of nervous system
  A Megalobladder and ureters 1 case, great improvement
  B Myelodysplasia with anesthesia of bladder 2 cases, 2 failures
  C Minimal old transverse myelitis 1 case, improved (residual absent, but other symptoms)
  D Diabetic neuropathy 1 case, much improved

From these data one may conclude that partial cystectomy will eliminate or greatly reduce residual urine in the presence of a hypotonic bladder if

1) There is no psychiatric cause of urinary retention
2) The sensory nerve supply is not hopelessly deficient
3) Mechanical obstruction is absent

In primary hypotonia and in neurogenic vesical dysfunction, the inherently defective detrusor may decompensate again after partial cystectomy if subjected to severe stress

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THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

ATONIC NEUROGENIC BLADDER IN PORPHYRIA

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Acute porphyria has long been a fascinating subject to the biochemist, but a diagnostic and therapeutic dilemma to the internist and a pitfall to the unsuspecting surgeon. Although a common and certainly a dramatic manifestation of the disease is the excretion of a red or port wine colored urine, porphyria has escaped emphasis in urologic literature. It is the purpose of this communication to add the finding of an atonic neurogenic urinary bladder to the already bizarre symptom complex seen in acute intermittent porphyria. To the author's knowledge, bladder atony has not previously been described as a symptom of this disease.

The porphyrins are a large group of compounds existing in nature in both a free and a combined state. They are characterized by a ring structure composed of four pyrrol nuclei joined by four methene bridges. In man, the porphyrins may be synthesized from succinate and glycine to provide prosthetic groups for the respiratory enzymes. The heme compounds (hemoglobin, myoglobin, cytochrome and catalase) are iron complexes of protoporphyrin 9, type 3.

The disease, porphyria, appears to represent a peculiar constitutional fault characterized by a disturbance of pyrrol metabolism resulting in the excretion of abnormal types and amounts of porphyrins and related substances in the urine. This metabolic abnormality is either the cause of, or associated with, definite clinical symptoms. Although many attempts to classify porphyria have been made, the most realistic seems to be that of Watson and his associates[1] based on the proposed site of origin of the abnormal porphyrins which ultimately appear in the urine.

This is as follows:

1) Porphyria erythropoietica—excessive and abnormal porphyrin formation in the bone marrow. Photosensitivity early in life, increased hemolysis and erythropoiesis, splenomegaly and red urine.

2) Porphyria hepatica—excessive and abnormal formation of porphyrins and porphyrin precursors in the liver, frequently with evidence of liver dysfunction.

   a. Intermittent acute porphyria—abdominal and/or nervous manifestations.
   b. Mixed porphyria—photosensitivity with or without abdominal and/or nervous manifestations.

The most commonly occurring form of porphyria is the intermittent acute type. Females are probably more commonly afflicted than males. Symptoms leading to diagnosis usually occur in the third or fourth decades of life, although

Accepted for publication July 20, 1955.

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milder symptoms occurring intermittently may have begun during adolescence. Characteristically, the disease occurs in individual attacks with varying periods of remission during which the patient may be entirely symptom-free. There are three major groups of symptoms and these may occur together or separately:

1) Systemic manifestations—abdominal pain, vomiting, constipation, hypertension, tachycardia and occasionally fever and leukocytosis.

2) Neuropathy—motor and sometimes sensory disturbances of the extremities, convulsions, syncope, bulbar palsy, coma and death by respiratory failure.

3) Psychic changes—agitation, delirium, hypochondriacal complaints and hallucination.

In acute porphyria the freshly voided urine is often pink to red or port-wine in color, especially during acute attacks. This finding should alert the careful observer to the possibility of this disease. However, even at the height of an attack, the urine may be clear, straw-colored, and still contain large amounts of porphyrin. Occasionally the dark color will develop when the urine is left standing a few hours. Although these color abnormalities of the urine are probably not due to porphyrin *per se* (though much of the dark color may be due to a porphyrin precursor, porphobilin), when they are present the physician is obligated to consider the possibility of porphyria. Actual diagnosis rests upon the laboratory demonstration of porphobilinogen or the Waldenstrom uroporphyrin, or both, in the urine. During remissions, however, these substances may be entirely absent from the urine.

CASE REPORTS

Case 1. T. T., a Caucasian woman aged 33, was first admitted to the Los Angeles County Hospital on October 29, 1954 for intestinal obstruction. A review of the patient's past history at that time revealed that she had been subject to periodic mental depression and hysterical behavior for many years. At one time she attempted suicide and was committed to a mental hospital. She had had nine major abdominal operations since 1942, four of these for the relief of intestinal obstruction. In retrospect, each operation had been preceded and followed by almost identical symptoms, principally abdominal pain, vomiting, pain in the legs and severe constipation. During the past year the pain in her abdomen had been almost continuous. In September 1953, during a severe attack of abdominal pain, she suddenly became unable to void voluntarily. This difficulty persisted for 3 weeks. Since then, there had been three more such episodes lasting from 1 to 3 weeks. During one of these episodes a cystoscopic examination was made. The patient was told nothing abnormal could be found.

One week prior to her entry here, she had been operated upon at another hospital for intestinal obstruction. However, no definite obstruction could be found. During the week prior to this surgery she had abdominal pain, vomiting and inability to voluntarily void her urine. Three days after the surgery all of the symptoms recurred.

Upon admission, the surgically scarred abdomen was moderately distended and diffusely tender. Peristalsis was hypoactive, but present. Gastrointestinal suction was instituted Two days later she became acutely hysterical Neurologic examination was entirely negative Sedation with heavy doses of barbiturates was attempted but appeared only to make her worse Acute intermittent porphyria was suspected and analysis of her urine revealed the presence of porphobilinogen (by the method of Watson and Schwartz) Upon questioning she denied ever having noticed dark urine but stated it had been a definite pink color on occasion

It was necessary to catheterize her daily for 2 weeks after admission before she was able to voluntarily empty her bladder An excretory urogram showed no abnormality One month after entry a cystometric study was done This showed a low pressure curve, a shift of the first desire to void to the right (400 cc) and a low intravesical pressure while attempting to void (fig 1) Cystoscopy revealed no abnormal findings The abdominal pain gradually subsided and she was finally discharged on December 17, 1954

She was readmitted to this hospital on January 6, 1955 with pain in the abdomen, legs and chest She was again unable to pass her urine and 400 cc were obtained by catheter A small amount of porphobilinogen was present in the urine She was placed on urecholine (bethanachol chloride) 5 mg every 4 hours by mouth A few days later she was able to void a small amount of urine The urecholine was continued for 2 weeks and during this time she was usually able to empty her bladder satisfactorily There was no subsequent evidence of urinary retention and she was able to leave the hospital, somewhat improved, on February 6, 1955

Case 2 L M , a Negress aged 37, was admitted to the Los Angeles County Hospital on January 19, 1955 complaining of right upper quadrant pain, nausea,

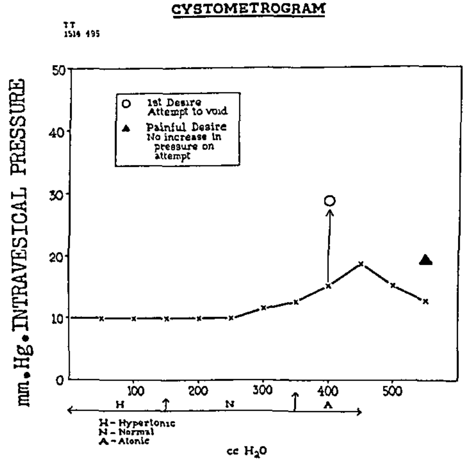

Fig 1 Case 1 Result of cystometric study

vomiting and pain in both thighs. These symptoms had been present for 2 weeks. In addition she stated her urine had been intermittently dark red, especially in the morning, for the past 6 weeks.

She had been admitted to this hospital on seven previous occasions with complaints of abdominal pain, vomiting, constipation, leg pains and fainting episodes. In March 1949 (her third admission) her urine was first noted to be dark red. The diagnosis of acute intermittent porphyria was established when large amounts of porphobilinogen and uroporphyrin were found to be present in the urine. She had two subsequent admissions that year for abdominal pain. In February 1952, she entered another hospital for abdominal surgical exploration. Dark red urine was noticed. The operation was cancelled and she was transferred to this hospital. Two days after entry she could not void and 600 cc of urine were obtained by catheter. This problem persisted for 6 days before she could void voluntarily. Her seventh admission was in February 1954 for the same complaints. Again she could not void and required catheterization for 4 days.

At the time of the present admission on January 19, 1955 the blood pressure was 150/100 and the pulse rate 132 per minute. There was no fever. The abdomen was soft and relaxed to palpation, although there was tenderness to deep palpation in the right upper quadrant. Peristalsis was decreased. Neurologic examination was negative except for some increase in the knee and ankle jerks.

She was unable to void upon entry to the hospital and stated she had been having difficulty in initiating her urinary stream for the past two days. When catheterized, 450 cc of very dark, almost coffee-colored, urine was obtained. This urine was strongly positive for porphobilinogen and uroporphyrin. The following day she was still unable to void and for this she was given urecholine 5 mg. every four hours by mouth. Two hours after the second dose she voided 300 cc urine without difficulty. The urecholine was continued for 2 days and thereafter there was no further evidence of urinary retention.

On her third hospital day, the administration of ACTH was begun, 80 mg. per day intramuscularly, for 3 days. This was accompanied by a remission of all symptoms, including a return of the blood pressure and pulse rate to her normal levels, and a marked reduction in the urinary porphyrin excretion. She remained asymptomatic and was discharged from the hospital 20 days after entry.

On February 28, 1955 as an out-patient, a cystometric study was done. This showed a low pressure curve, a somewhat delayed initial desire to void (250 cc) and a low maximal voluntary pressure (20 mm. Hg).

DISCUSSION

Two cases of acute intermittent porphyria are presented in which urinary retention appeared to be a part of the acute porphyric attacks. The results of the cystometric studies are consistent with the diagnosis of an atonic neurogenic bladder. No obstructive uropathy could be found. Since some evidence of peripheral neuropathy is common in acute intermittent porphyria,[2] it is suggested that the atonic bladder in these patients was a manifestation of porphyric involvement of the autonomic nervous system It is interesting that no other evidence of neuropathy was observed in either of these patients However, in case 2, hypertension was present and Kezdi[3] has suggested that the transient hypertension in acute porphyria may be secondary to porphyric polyneuritis Involvement of the autonomic nervous system has been suggested as one cause of the abdominal pain in porphyria,[1] and an unidentified pigment deposition in autonomic ganglia has been observed at necropsy [4] On the basis of the similarity of the x-ray findings of the gastrointestinal tract in acute intermittent porphyria to those seen after vagotomy, Berlin and Cotton[5] have suggested involvement of the parasympathetic nervous system to explain some of the visceral symptoms of acute porphyria An atonic neurogenic bladder appears to be additional evidence of autonomic nervous system involvement in porphyria

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In a case of acute porphyria presented by Roston,[6] one of the early presenting symptoms was difficulty in starting the urinary stream Bladder neck obstruction was suspected Cystoscopy showed nothing abnormal However, the bladder urine was noted to be dark, reddish brown, and when found to be positive for porphobilinogen led to the diagnosis of porphyria Hart and Collard[7] reported a case of acute porphyria where the initial examination of the patient revealed the bladder to be painlessly distended to the umbilicus Later, flaccid paralysis developed and the patient died from respiratory failure. The author is aware of another, as yet unreported, case of acute porphyria with severe bladder atony, followed by recovery, occurring during the first week of the initial attack [8]

A good therapeutic response was obtained in both of our cases following the use of urecholine, a parasympathomimetic drug Boone[9] stated that the most responsive individuals to urecholine are those with temporarily hypotonic detrusors secondary to neuropathies amenable to therapy or spontaneous remission The neurogenic bladder of porphyria would appear to be of the latter type

SUMMARY AND CONCLUSIONS

Two cases of acute intermittent porphyria are presented in which transient urinary retention occurred during acute porphyric attacks This was interpreted as resulting from an atonic neurogenic bladder secondary to porphyric neuropathy Although there is evidence for autonomic nervous system involvement in many cases of acute porphyria, an atonic neurogenic bladder has not previously been described in this disease

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THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

ILEAL LOOP DIVERSION: ITS APPLICATION TO THE TREATMENT OF NEUROGENIC BLADDER DYSFUNCTION

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Most patients with neurogenic bladder dysfunction from any cause may be treated conservatively by conditioning, transurethral resection of the bladder neck, pudendal neurectomy, or occasional sacral neurectomy. There are individuals, however, with upper motor neuron lesions who experience such unsatisfactory reflex bladder function that it is impossible to keep them dry. Other patients with lower motor neuron lesions, in spite of fairly satisfactory voiding, probably because of lack of normal accommodation to filling and constantly high bladder pressure, suffer reflux and upper urinary tract complications of pyelonephritis, calculi, and hydronephrotic atrophy.

Male patients may be satisfactorily treated by indwelling catheter or condom drainage after resection of the bladder neck or other procedures that have not corrected the situation. Female patients, however, present a serious problem of urine collection because of leakage about the catheter. No satisfactory mechanism has been devised to collect urine from the incontinent female.

Permanent cystostomy and vesical neck exclusion would appear to be the simplest procedure, but as in one of the cases to be presented it did not solve the problem. Some other type of urinary diversion becomes necessary. Uretero-enterostomy to the intact sigmoid is out of the question because of upper urinary tract damage and rectal incontinence. Cutaneous ureterostomy or nephrostomy is fraught with troubles and almost always results in gradually impaired renal function due to persistent infection, calculus formation and difficulty in reintroducing tubes which often necessitate re-operation. Free drainage diversion without tubes or catheters would seem to be the solution.

We have, therefore, elected to try urinary diversion in selected cases by fashioning a free-draining ileal loop into which the ureters have been transplanted using a direct end-to-side anastomosis essentially as described by Bricker.[1, 2] Recently, Hansen, Eggers, Bill, and Dillard[3] reported the use of this procedure in the treatment of urinary incontinence in two patients with congenital abnormalities—exstrophy and myelomeningocele. The method has been used by us in the treatment of 4 patients. These cases are presented not only to illustrate use of this particular technique but to call attention to the problems involved in treating this type of patient. Urine collection has been best accomplished by the use of the Rutzen bag. By and large, this has proved satisfactory.

Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23–25, 1955.

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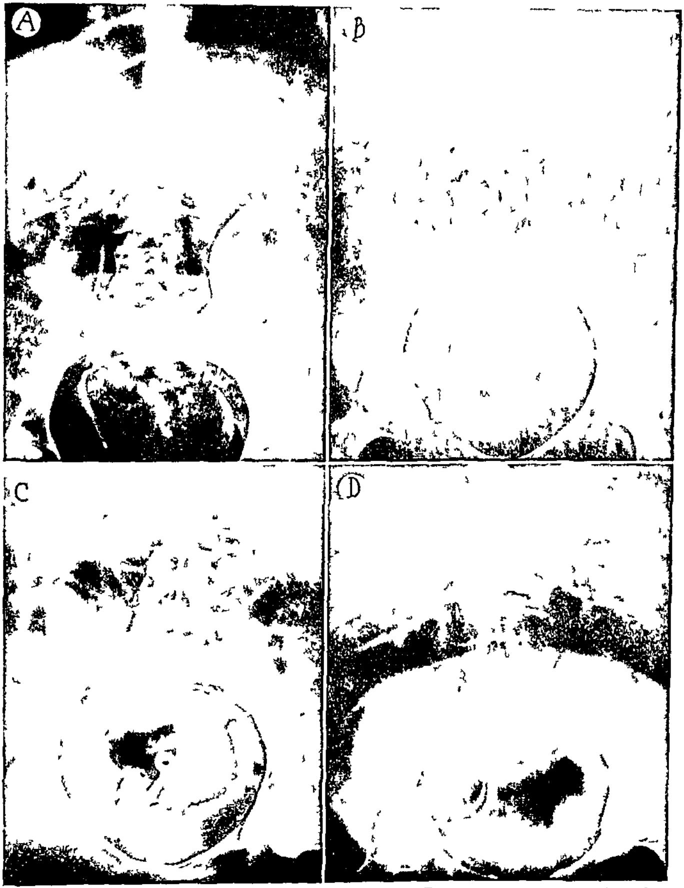

FIG 1 Case 1 *A*, retrograde pyelogram on admission *B*, excretory urogram after closure of vesical neck and suprapubic cystostomy (3 hour film) Note degree of hydroureter and hydronephrosis *C*, injection of dye into bladder through suprapubic tube to demonstrate reflux into ureters *D* excretory urogram 5 months after ileal loop procedure Marked improvement in appearance of renal pelves is apparent

CASE REPORTS

Case 1 M J , M G H No 866571 A 25 year-old female paraplegic was admitted to the Massachusetts General Hospital in July 1954 for rehabilitation Eight years prior to admission she had fallen and suffered a back injury resulting in complete paralysis below the the T10 segment Laminectomy was done, but there was no return of sensation or motor power She spent 2 years in another hospital where attempts at bladder conditioning were unsuccessful. Catheter drainage was complicated by the development of a vesico-urethro-vaginal fistula which made urine collection impossible. Continuous wetness resulted in numerous ulcers over the sacrum and about the perineum and upper thighs for which various plastic procedures had been carried out. For some time no effort at all had been made to collect urine.

Physical examination revealed a thin, complaining, odiferous patient who appeared chronically ill. There were multiple scars and ulcers about the perineum, upper thighs and over the sacrum. A vesicovaginal fistula was palpated 1½ inches in diameter involving the bladder neck. There was complete paralysis and complete loss of sensation below the umbilicus.

Laboratory studies showed anemia, normal blood chemistry values, and many white blood cells in the urine. An intravenous urogram and retrograde pyelogram showed good kidney function and changes suggestive of chronic pyelonephritis (fig. 1, *A*). Cystoscopy confirmed the size and location of the vesicovaginal fistula. It appeared that the floor of the bladder neck and urethra had sloughed.

Before any attempt could be made to treat the various ulcers it was apparent that some form of urinary diversion was necessary. Therefore, on July 28, 1954 the bladder neck was divided, separated from the vagina, closed, and a cystostomy established. Following this procedure the suprapubic tube drained well. The vaginal leakage disappeared. Many of the ulcers about the perineum and over the sacrum healed. However, intravenous urograms showed progressive bilateral hydroureter and hydronephrosis and impairment of renal function (fig. 1, *B*). It was at first thought that ureteral obstruction had developed as a result of trauma incident to dissecting up the bladder neck or to periureteritis, but a cystogram (fig. 1, *C*) demonstrated reflux from the bladder into both ureters. It was therefore concluded that damage to the parasympathetic nerves had occurred as a result of disturbance of the floor of the bladder which somehow affected delivery of urine to the bladder. At any rate, the presence of pyelonephritis and rapidly failing renal function made further diversion necessary. After discussing the pros and cons of cutaneous ureterostomy and nephrostomy, since ureterosigmoidostomy was out of the question, it was decided to fashion an ileal loop. This was done on September 17, 1954. At that time no obstruction could be demonstrated in either lower ureter. Cystectomy was done at the same time to eliminate an otherwise chronically infected pouch. Her postoperative period was somewhat stormy but ultimate recovery was good and renal function has returned to a surprising degree. A recent excretory urogram is shown in figure 1, *D*. There is slight residual hydronephrosis, particularly on the left. No attacks of pyelonephritis have occurred. The sacral ulcers are being treated and are responding well. Patient is undergoing rehabilitation with braces.

Case 2. M. W., M.G.H. No. 306555. A 38-year-old nurse was first seen by one of us (W. F. L.) in October 1948. In 1938 operation for herniated lumbar intervertebral disc was done. Pain continued thereafter and 4 years later first a unilateral and then bilateral chordotomy were done. The result of these procedures was unsatisfactory in that only spotty anesthesia was present, moderate weakness of muscles in both lower extremities developed, and worst of all a spastic reflex bladder and rectal incontinence developed

Study in the hospital showed a normal upper urinary tract and spastic reflex bladder with maximum capacity of 80 cc Voiding of 30 to 50 cc occurred frequently and irregularly Tidal drainage did not modify bladder function The patient was discharged to use an indwelling catheter at night so that she could sleep undisturbed It became evident that this was no solution to the problem and the patient was readmitted to the hospital for further study Cystometric study was done after blocking the sacral nerves which showed immediate improvement in vesical capacity, absence of reflex activity until near normal capacity was reached Therefore, on January 24, 1949, through a low abdominal incision, the pelvis was explored and part of the parasympathetic nerve supply to the right side of the bladder was divided Change in bladder function was quite remarkable in that she could hold urine for two to three hours and voided 150 cc urine each time Residual urine was less than 100 cc

The effect of this procedure was short lived in that by July 1949 she was voiding as frequently as before and bladder capacity was 100 cc or less Her condition gradually reverted to that before operation Therefore, in November 1949 the patient was readmitted to the hospital Cystometric studies before and after novocain block of the sacral nerves demonstrated reversion from reflex irritable bladder with capacity of 90 cc to capacity of 400 cc without reflex activity Furthermore, after block the patient was able to void without difficulty Excretory urograms were again normal On the basis of this the patient was operated on again November 7, 1949 through a midline incision After identification of the second, third and fourth sacral nerves deep in the pelvis behind the hypogastric vessels, rami were found passing to the bladder pedicles, all of which were sectioned and portions removed After operation patient's urinary function became almost normal Cystometric study showed capacity of 250 cc with slight tendency to hypertonicity The patient was completely continent and voided from 150 to 200 cc each time Over a period of 1 year her bladder function gradually deteriorated again, bladder capacity diminished, frequency recurred, and stress incontinence became troublesome Finally, since the patient was working, she was placed on constant catheter drainage

She was readmitted on March 16, 1951 with acute right pyelonephritis Excretory urograms were again normal Bladder capacity was found to be 100 cc again Block of sacral nerves at this time showed no effect on bladder function indicating that there had been no regrowth of parasympathetic nerves The patient was miserable on catheter drainage so that suprapubic cystostomy was done on March 29, 1952 This did not prevent urethral leakage and made the patient uncomfortable On September 23, 1952 this was closed and urethral catheter drainage reinstituted The situation became intolerable because of leakage about the catheter and encrustation

Therefore, the patient was readmitted on June 17, 1953 and after considerable discussion it was felt that enlargement of the bladder might help, and on cystitis on the right side of the bladder. From then until the fall of 1954 the patient had had intermittent treatment with only partial or temporary relief. Finally, she was admitted to the Roger Williams Hospital in Providence, Rhode Island. Her surgeon felt that presacral neurectomy might help and this was performed removing not only the presacral nerves but lateral pelvic tissue which must have included at least a portion of the hypogastric plexus and the parasympathetic nerves, because afterward the patient was completely relieved of pain but voided with difficulty and began to have discomfort in both kidney regions associated with fever. Excretory urography, which had previously been normal (fig. 4, *A*), showed marked bilateral hydroureter and hydronephrosis (fig. 4, *B*). The senior author was called to see the patient at this time and recommended catheter drainage because of a large volume of residual urine and serious damage to the upper urinary tract. After an indwelling catheter had been placed the temperature gradually returned to normal and excretory urograms later showed improvement in the degree of hydroureter and hydronephrosis. It was apparent that the patient either had to be placed on catheter drainage, cystostomy, or some other form of urinary diversion. After discussion with the patient ileal loop diversion was decided upon and operation carried out on January 3, 1955. The bladder was removed at the same time. Convalescence was stormy with distention and vomiting. Finally, it became obvious that small bowel obstruction was present. Re-operation was carried out and a loop of small bowel found adherent to the base of the ileal loop. The patient died following this procedure. During the time patient lived there was never any difficulty with the collection of urine from the loop and patient was free of any indication of upper urinary tract complications.

Case 4. H. F., M.G.H. No. 716434. A 48-year-old married woman was first seen in May 1952 complaining of urinary incontinence. Twenty years previously radiation therapy had been given to a plantar wart on the sole of the left foot. The area never healed properly so that over the years treatment consisting of skin grafts, pedicle grafts, lumbar sympathectomy, and finally transmetatarsal amputation were done to get a usable foot. None of these procedures succeeded. Pain became a problem. Finally, unilateral chordotomy was done in 1951 with relief of pain. However, when the patient became active again the skin over the amputation stump broke down and pedicle graft again was tried but infection in and about the graft with ascending lymphangitis developed. Worst of all, after chordotomy, neurogenic bladder dysfunction developed so that patient dribbled urine frequently and carried 250 cc of residual urine. Even catheter drainage would not keep her dry since urine was frequently passed about the catheter. Attempts to modify bladder behavior by tidal drainage were unsuccessful. Cystoscopy showed nothing. Cystometric study demonstrated an extremely hyperactive reflex bladder.

Finally, the patient was admitted for study on December 22, 1952. Blocking of sacral nerves and studies of bladder function were done. These seemed to show that when the left sacral roots were blocked, function became more normal. Resection of the left parasympathetic nerves was done on December 24, 1952

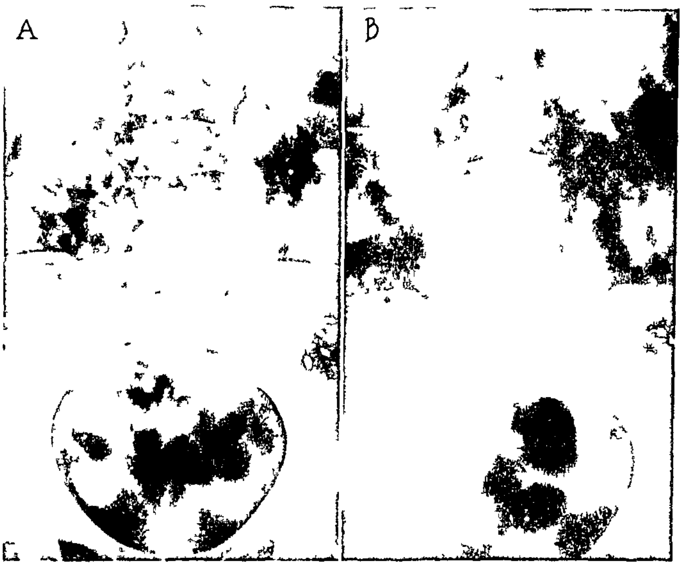

FIG 5 Case 4 *A* excretory urogram February 1954 *B*, excretory urogram after ileal loop diversion

The patient could not void after this and the only benefit derived was that she could stay dry on urethral catheter drainage Neurological examination after this suggested an underlying disease such as multiple sclerosis During the next 2 years she was carried along on indwelling catheter drainage Attempts on several occasions to revert to normal voiding were unsuccessful

During the spring of 1954 the skin over the left foot eroded, became infected and was associated with lymphangitis This recurred each time activity was begun Finally, amputation of the left leg below the knee was done and prosthesis fitted So far, it appears that the skin of the stump will be able to withstand irritation of the artificial limb Bladder drainage by catheter became completely unsatisfactory because of incrustation, leakage, and chronic irritation with bleeding The patient was admitted for the last time in February 1955 Excretory urography (fig 5, *A*) showed normal upper urinary tract Cystoscopy revealed a contracted bladder with marked chronic inflammatory changes An ileal loop into which both ureters were transplanted was fashioned and the bladder excised The patient made a good recovery and for the first time in 5 years is comfortable and free from catheter and urine leakage The postoperative excretory urogram is shown in figure 5, *B*

DISCUSSION

One may justly criticize the handling of these cases, yet we are sure that anyone who has come to grips with rehabilitation of individuals afflicted with this type of neurogenic bladder dysfunction will view our efforts with a certain amount of charity.

Our own analysis of the cases is somewhat as follows. The cystostomy and vesical neck exclusion performed on the first patient resulted in damage to parasympathetic nerves that should not have occurred. However, the defect in the bladder neck necessitated considerable dissection about the bladder base in order to effect closure of the fistula. The resulting ureteral reflux, hydroureter and hydronephrosis with rapidly diminishing renal function in the presence of a freely draining cystostomy tube are difficult to explain. Perhaps lower ureteral peristalsis was interrupted by nerve section or damage. One might have solved the problem by skin ureterostomies performed through pedicle flaps as described by Talbot et al.[4] Cystectomy would have been necessary to be rid of the chronically infected vesical pouch. We elected ileal loop diversion because it offered one stoma, freedom from catheters, and the hope of freer drainage. The result thus far after 9 months seems quite satisfactory.

The procedures utilized in treating the second patient seem poorly chosen and redundant. There seemed, however, to be good basis for denervation of the bladder. The utilization of two procedures was inexcusable, yet we were not familiar with the procedure and found no precedent to guide us. At last we developed a technique which allows denervation of the bladder without damage to the sacral nerve routes. This, in a patient without paraplegia, would have resulted in further weakness of pelvic girdle and leg muscles. Perhaps the subsequent contraction of the bladder may have been prevented if we had been aware that this would occur. Interval dilatation could have been tried. It was interesting to note that after denervation of the bladder its outline by cystogram was smooth and normal and the patient voided almost normally. Only small amounts of residual urine were present. This may be compared with the cystogram in case 3 after partial denervation of the bladder which shows marked irregularity and asymmetry. The use of the cecal pouch was a frank experiment which did not solve the problem because it decompensated. No hyperchloremia was noted. Repeated attacks of right pyelonephritis uncontrollable by medication, undoubtedly due to right ureteral reflux, forced us into some type of urinary diversion. Again ureterostomy seemed less satisfactory than the ileal loop which has worked well. The only remaining complaint is collection of purulent material in the bladder which is irritating and unpleasant. Cystectomy should have been done.

Patient 3 presented the same problem as patient 1 in that hydroureter, hydronephrosis and pyelonephritis rapidly followed partial denervation of the bladder. The bladder outlined by the cystogram shows a smooth, symmetrical vesical neck and base while the vertex is very irregular and asymmetrical. This suggests to us that the only remaining portion of the bladder normally innervated was the right half of the vertex. This same cystographic appearance was noted during the war (by W. F. L.) after partial cauda equina lesions resulting from wounds.

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[4] Talbot, H. S., Paull, D. P. and Read, G. R.: Late complications of paraplegia III. Treatment of vesicoureteral reflux by skin ureterostomy through a pedicle flap. J. Urol., **70:** 216, 1953.

The question arises in regard to partial parasympathetic nerve lesions whether the part with deficient or absent innervation could be removed and leave a normally functioning bladder. This requires further investigation. This patient's death after release of intestinal obstruction was tragic. It simply points out one of the possible complications of the ileal loop operation which is occasionally bound to occur, must be watched for and corrected early. The loop functioned perfectly with no leak or ureteral obstruction. Perhaps we should have tried a longer period of catheter drainage and transurethral resection of the bladder neck but since bilateral reflux was present it seemed best to use a procedure which would solve the whole problem. Hutch's operation[5] would have corrected only one aspect of the problem.

The fourth patient presented problems similar to patient 2—unsatisfactory reflex bladder function after chordotomy and in the presence of intrinsic pyramidal tract disease (multiple sclerosis). Denervation of the bladder was completely unsuccessful in terms of function. Incontinence and retention were both present.

Our experience to date suggests that this procedure has a place in the rehabilitation of certain patients with unsatisfactory neurogenic bladder dysfunction. Bricker's and Cordonnier's[6] experience of more than five years leads us to feel that if the ileostomy stoma is properly fashioned by excising a circular patch of skin, subcutaneous tissue and fascia, the loop will drain freely without holding urine. This is a most important technical point. If urine pools in the loop with direct ureteroileal anastomosis, reflux and pyelonephritis may be expected to occur. Perhaps a valve should be fashioned as in the performance of ureterosigmoidal anastomosis.

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[5] Hutch, J. A. Vesico ureteral reflux in the paraplegic. Cause and correction. J. Urol. 68: 437, 1952.

[6] Cordonnier, Justin J. Personal communication.

THE JOURNAL OF UROLOGY
Vol 75, No. 3, March 1956
Printed in U.S A.

A STUDY OF 2678 PATIENTS WITH INITIAL CARCINOMA OF THE BLADDER: I. SURVIVAL RATES

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In the quarter of a century since the Bladder Tumor Registry was established by the American Urological Association at the Army Medical Museum (now the Armed Forces Institute of Pathology) clinical records and microscopic slides from more than 6,000 patients with bladder tumors have been collected. The group selected for the present study comprises patients who sought urologic advice for the first time, were found to have a primary bladder tumor without demonstrable metastasis, and were treated for tumor. The study was further limited to those patients who had been treated in 1945 or earlier (thus allowing at least 5 years of observation since the initial treatment) and those who survived the initial therapy. The study differs therefore from the earlier report[1] which included all patients registered before 1936. A comparison of the clinical behavior of patients with carcinoma of the bladder registered prior to the advent of modern chemotherapeutic and antibiotic agents with those registered since then would be of interest and will be the subject of another study.[2]

Although selected from the Registry material, which itself is highly selective, the present series represents a homogeneous group of patients. Care must be exercised, however, in applying the data obtained in this study to everyday practice as the patients are obviously ideal.

The purpose of this study is to 1) evaluate the five-year "tumor-free" rate, and 2) the annual survival rates irrespective of the presence or absence of the tumor.

MATERIAL AND METHODS

On the basis of the criteria outlined, 2678 patients were selected for this study, including 935 of the 1400 previously reported in 1951.[1] Clinical summaries, microscopic slides and followup information were available for all these patients. Although more than one-third of the cases included in the present study are from the earlier report[1] the results of the two studies are not comparable as they utilize material of different types.

Every diagnosis was based on microscopic examination, but only about half the cases were re-examined in 1951, most of these being from the 1951 report. The diagnostic criteria were those of the old Registry classification* re-stated in the 1951 report.

Accepted for publication July 29, 1955.

[1] DEAN, A. L., MOSTOFI, F. K., THOMSON, R. V. AND CLARK, M. L.: A restudy of the first 1400 tumors in the Bladder Tumor Registry, J. Urol., **71**: 571–590, 1954.

[2] MOSTOFI, F. K., THOMSON, R. V. AND DEAN, A. L., JR.· Mucinous' adenocarcinoma of the bladder. Cancer, **8**: 741–758, 1955.

* The new Registry classification instituted in 1952 attempts to distinguish papillomas and to base the diagnosis entirely on microscopic findings, without regard to size, multiplicity or recurrence of the tumor.

Briefly summarized, all epithelial tumors of the bladder were classified as carcinoma. Grade 1, if they were well differentiated, less than 2.5 cm. in base diameter, and single, grade 2, if less well differentiated and/or infiltrating, multiple, over 2.5 cm. in base diameter, and/or recurrent, and grade 3, if undifferentiated. According to this classification most of the "papillomas" were placed in the grade 1 papillary carcinoma group and all grade 4 (Broders) carcinomas were included in grade 3. Although the classification did consider size, number and recurrence, since such information was not always available, the diagnosis in many cases was based on histologic features alone. In this study no distinction has been made between transitional cell carcinoma and squamous cell carcinoma, but adenocarcinomas have been excluded as they are the subject of a separate report.[2]

Since "papillomas" were included with grade 1 carcinoma, the material has been separated into various diagnostic categories so as to give a clearer idea of the behavior of each grade.

The study was facilitated by numerical coding and entry on punch cards of all available data in the Registry forms.

CLINICAL DATA

Thirty-three per cent of the patients were in the age group of 60–69, 29 per cent in 50–59, 76 per cent were in the age group of 40–69, 92 per cent in 40–79. Only 5 patients in the series were in the 10–19 year group and only 3 in the 90–99.

A comparison of the average age and sex of patients in each diagnostic group showed that the 854 men with papillary carcinomas, grades 1 and 2, were definitely from a younger group than the 232 women with similar tumors. The average age of 1086 patients with noninfiltrating carcinomas was distinctly lower than that of the 1548 patients with infiltrating tumors—57 compared to 60 (table 1).

Of 1101 patients with noninfiltrating carcinoma, 869 were male and 232 female, of 1572 patients with infiltrating tumors, 1158 were male and 414 female. In other words, of 100 tumors occurring in male patients, 43 were noninfiltrating

TABLE 1 *Number, average age and sex of 2634* patients with initial carcinoma of the bladder for each diagnostic group*

Diagnostic Group and Grade	Number of Patients			Average Age		
	Total	Male	Female	Combined	Male	Female
Total	2634	1994	640	59	59	61
Noninfiltrating	*1086*	*854*	*232*	*57*	*57*	*60*
Papillary I	332	261	71	53	52	58
Papillary II	754	593	161	59	59	60
Infiltrating	*1548*	*1140*	*408*	*60*	*60*	*61*
Papillary and infiltrating II	668	502	166	60	60	61
Papillary and infiltrating III	343	260	83	62	61	64
Infiltrating II and III	537	378	159	60	60	59

* Excludes 39 patients whose age was not stated, 1 whose age and sex were unknown, and 4 whose sex was not known

TABLE 2. *Distribution of noninfiltrating and infiltrating initial carcinomas of bladder in relation to sex*

Diagnostic Group	Number			Per Cent		
	Male	Female	Total	Male	Female	Total
Noninfiltrating	869	232	1101	43	36	41
Infiltrating .	*1158*	*414*	*1572*	*57*	*64*	*59*
Total	2027	646	2673	100	100	100

and 57 were infiltrating; of 100 tumors occurring in female patients only 36 were noninfiltrating and 64 were infiltrating. Although infiltrating carcinoma of bladder was more prevalent than noninfiltrating type in both male and female patients in this series, it is likely to be infiltrating in a relatively larger proportion of female than of male patients (table 2).

Forty-one per cent of the tumors were papillary noninfiltrating, 39 per cent were papillary and infiltrating, and 20 per cent were nonpapillary sessile-nodular infiltrating (table 3). Thus 80 per cent of the tumors were papillary. It may be noted that only 13 per cent of the group were papillary carcinoma, grade 1. This may indicate either that the Registry tends to assign a higher grade of malignancy to the tumors that are received, or that more tumors of higher grades of malignancy are registered. However the downward progression of survival rates with increasing malignancy, as shown in the latter part of this paper, leaves little doubt that most of the tumors were properly graded.

Considering the 2678 patients as a whole, 34 per cent had single tumors limited to one area, 37 per cent had single tumors involving more than one area (e.g., the trigone and the posterior wall), and 24 per cent had multiple tumors in one or more areas (table 4). In the last category there were 109 patients who had multiple tumors confined to one area, 546 patients with tumors in more than one area, and 6 patients with no information as to areas involved. Thirty-five per cent of the papillary noninfiltrating tumors were limited to single areas, while 41 per cent of infiltrating tumors involved more than one area.

Because of the discrepancies inherent in reporting the exact sites of the tumors, it was believed that localization was reliable only for single tumors limited to single areas. Forty-seven per cent of these were in the lateral walls, 21 per cent in the trigone, 18 per cent in the posterior wall, 8 per cent in the anterior wall, and

TABLE 3. *Distribution of various grades of carcinoma in 2678 patients*

Diagnostic Group and Grade	Number	Per Cent
Noninfiltrating	*1104*	*41.*
Papillary I.	343	13.
Papillary II.	761	28.
Infiltrating	*1574*	*59.*
Papillary and infiltrating II	682	26.
Papillary and infiltrating III	349	13.
Infiltrating II and III.	543	20.

TABLE 4 *Distribution of noninfiltrating and infiltrating initial carcinoma of the bladder as to number of tumors and number of areas involved*

Number and Area Involved	Type of Carcinoma					
	Total		Noninfiltrating		Infiltrating	
	Number	per cent	Number	Per cent	Number	per cent
Total	2678	100	1104	100	1574	100
Single tumor, 1 area	900	34	386	35	514	33
Single tumor, more than 1 area	995	37	344	31	651	41
Multiple tumors, 1 or more areas	661	24	324	29	337	21
Unknown as to multiplicity	122	5	50	5	72	5

TABLE 5 *Site of origin of single carcinomas involving one area of the bladder*

Diagnostic Group and Grade	Number of Patients	Site of Origin Per Cent				
		Bladder wall			Trigone*	Vault
		Lateral	Anterior	Posterior		
Total	900	47	8	18	21	6
Noninfiltrating	*386*	*52*	*6*	*20*	*19*	*3*
Papillary I	148	50	4	26	18	2
Papillary II	238	53	7	16	20	4
Infiltrating	*514*	*43*	*9*	*17*	*23*	*8*
Papillary and infiltrating II	221	48	6	17	25	4
Papillary and infiltrating III	89	40	13	18	18	11
Infiltrating II and III	204	39	10	16	24	11

* "Trigone" includes trigone, ureteral orifice and/or bladder neck

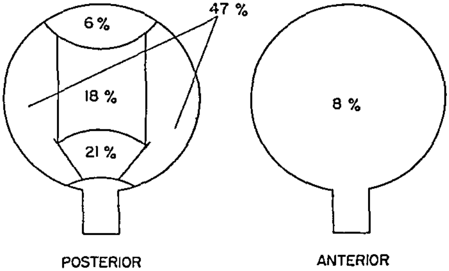

FIG 1 Initial carcinoma of bladder Diagrammatic sketch of bladder showing relative distribution of single carcinomas involving single areas "Trigone" includes trigone, ureteral orifices and/or bladder neck

6 per cent in the vault (table 5, fig 1) Whereas only 2 per cent of the papillary noninfiltrating grade 1 carcinomas occurred in the vault, 11 per cent of the infiltrating grades 2 and 3 carcinomas were in this area of the bladder Statistical tests indicated that most of the noninfiltrating tumors occurred in the lateral walls, and most of the tumors occurring in the dome were infiltrating

In 240 patients the tumor was confined to the trigone. 193 of these had single

TABLE 6. *Trigone* involvement in 2611† patients with initial carcinoma of the bladder*

Area Involved	Type of Carcinoma					
	Total		Noninfiltrating		Infiltrating	
	Number	Per cent	Number	Per cent	Number	Per cent
Total with site stated	2611	100.	1065	100.	1546	100.
Trigone alone	240	9.	96	9.	144	9.
Trigone with other areas	1088	42.	381	36.	707	46.
Other areas not involving trigone	1283	49.	588	55.	695	45.

* "Trigone" includes trigone, ureteral orifices and/or bladder neck.

† Excludes 67 cases unknown as to the areas involved.

tumors, 35 had multiple tumors and in 12 it was not known whether the tumors were single or multiple, but it was known that they were limited to the trigone (table 6). In addition, 1088 other tumors either originated in or involved the trigone (669 single carcinomas which had involved more than one area of the bladder, 393 multiple tumors which were in more than one area, and 26 unknown as to number, but known to involve more than one area). Thus, although only 21 per cent of single tumors in single sites arose in the trigone, when all cases in which the tumor site was known were considered, 51 per cent involved the trigone either alone or with other areas. Fifty-five per cent of the tumors involving the trigone were infiltrating; 45 per cent were noninfiltrating.

SURVIVAL DATA

The 2,678 cases in this study could be subdivided into two categories: the determinate, comprising 2,023 and the indeterminate, comprising 655. The determinate category included 569 5-year "tumor-free"* patients and 1,454 failures. In the 569 5-year "tumor-free" patients were a) 484 patients (391 alive and 93 dead) without recurrence at any time during the 5 years or more following initial therapy; b) 30 alive with first recurrence or metastasis 6 years or more following initial therapy; c) 15 dead with first recurrence or metastasis 7 years or more after initial therapy; d) 8 alive with no mention of tumor at the last followup, 6 years or longer without interim recurrence; e) 32 dead with no mention of tumor at the last followup, 7 years or longer, but without interim recurrence.

The 1,454 failures included a) 167 patients alive with recurrence at 5 years or less; b) 969 patients dead with recurrence at 6 years or less, and c) 318 patients (194 alive and 124 dead) 6 years or longer, who had one or more recurrent tumors. The 655 in the indeterminate category included a) 240 patients (142 living and 98 dead) without tumor or metastasis at 4 years or less, b) 352 patients (36 living and 316 dead) with no followup details as to tumor or metastasis, and c) 63 dead with no information as to the time interval between operation and death.

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* The term 5-year "tumor-free", employed to indicate no reported tumor or metastasis, is based on reports by physicians and/or correspondence with patients who stated that there were no symptoms or subsequent treatment for at least 5 years following initial treatment. Admittedly, a factor of error probably exists here, but in these cases this was the most accurate information available.

Thus the 5-year "tumor-free" and the "treatment failure" rates for the entire group were 28 per cent and 72 per cent, respectively. It should be noted that these rates are not comparable with those reported in 1951, because the present report concerns itself only with patients who had initial carcinoma of the bladder, who had no metastasis at the time of first admission and who were treated for the tumor.

In 569 (28 per cent) of the 2,023 patients who had been treated prior to 1945 and for whom data were available no tumor or metastasis was evident for at least 5 years after the initial treatment (table 7). Three hundred and fifty-eight patients (42 per cent) with noninfiltrating carcinoma (papillary, grades 1 and 2) were "tumor-free" as compared to 211 of the 1168 patients (18 per cent) with infiltrating carcinoma who were "tumor-free." The percentage of "tumor-free" patients decreased from 54 per cent for papillary carcinoma, grade 1, to 14 per

TABLE 7. *Survival without demonstrable recurrence and/or metastasis five years following initial treatment*

Diagnostic Group and Grade	Total With Data*	No Reported Tumor†	
		Number	Per cent
Total	2023	569	28.
Noninfiltrating	*855*	*358*	*42.*
Papillary I	264	142	54
Papillary II	591	216	37.
Infiltrating	*1168*	*211*	*18.*
Papillary and infiltrating II	518	121	23.
Papillary and infiltrating III	272	37	14.
Infiltrating II and III	378	53	14.

* Excludes 655 patients with incomplete data.

† Based on reports by physicians and correspondence with patients who stated that there were no symptoms or subsequent treatment for tumor for a period of 5 years or longer following initial treatment.

TABLE 8. *Survival without demonstrable recurrence and/or metastasis of bladder tumors ten years following initial treatment*

Diagnostic Group and Grade	Total With Data*	No Reported Tumor†	
		Number	Per cent
Total	1502	257	17.
Noninfiltrating	*576*	*153*	*27.*
Papillary I	168	59	35.
Papillary II	408	94	23.
Infiltrating	*926*	*104*	*11.*
Papillary and infiltrating II	400	59	15.
Papillary and infiltrating III	210	23	11.
Infiltrating II and III	316	22	7.

* Excludes 708 patients with incomplete data.

† Based on reports by physicians and correspondence with patients who stated that there were no symptoms or subsequent treatment for tumor for a period of 10 years or longer following initial treatment.

TABLE 9. *Survival without demonstrable recurrence and/or metastasis of bladder tumor fifteen years following initial treatment*

Diagnostic Group and Grade	Total With Data*	No Reported Tumor†	
		Number	Per cent
Total .	734	61	8.
Noninfiltrating	*240*	*31*	*13.*
Papillary I	53	10	19.
Papillary II	187	21	11.
Infiltrating . . .	*494*	*30*	*6.*
Papillary and infiltrating II	186	14	8.
Papillary and infiltrating III ..	82	4	5.
Infiltrating II and III	226	12	5.

* Excludes 444 patients with incomplete data.

† Based on reports by physicians and correspondence with patients who stated that there were no symptoms or subsequent treatment for tumor for a period of 15 years or longer following initial treatment.

cent for infiltrating carcinoma, grades 2 and 3. Thus four times as many patients with papillary carcinoma, grade 1, were alive without tumor as were patients with infiltrating carcinoma, grades 2 and 3. While the 5-year "tumor-free" rate was 42 per cent for those with noninfiltrating, and 18 per cent for those with infiltrating tumors, the corresponding percentages for the 1502 patients in the 10-year group were 27 and 11 (table 8), and for the 734 patients in the 15-year group, 13 and 6 (table 9). The percentages of "tumor-free" patients with papillary carcinoma, grade 1, for 5, 10 and 15 years were 54, 35 and 19, respectively, in contrast to those with infiltrating carcinoma, grades 2 and 3, which were 14, 7 and 5. It must be realized that the 569 "tumor-free" patients in the 5-year group included also the 257 in the 10-year group and the 61 patients in the 15-year group. Each group was "exposed to all risks of surviving 5, 10 or 15 years" and thus in each there was a chance of survival for the specified period; for instance, the 10-year group included all those patients treated in 1940 or earlier while the 15-year group included only those treated before 1935. Cognizance should also be taken of the lower average age of patients with noninfiltrating tumors in comparison with patients having infiltrating tumors.

For the 2615 patients with initial carcinoma of the bladder (2678 minus 63 for whom the interval between treatment and death was unknown), regardless of the grade of the tumor, the survival rate for 1 year was 76 per cent; for 5 years, 49 per cent, and for 10 years, 35 per cent (fig. 2). When the rates were analyzed for each grade, the 334 patients with papillary carcinoma, grade 1, showed a 1-year survival rate of 96 per cent, a 5-year survival rate of 85 per cent, and a 10-year survival rate of 67 per cent. The survival rate decreased with increasing degrees of malignancy so that for 529 patients with infiltrating carcinomas, grades 2 and 3, the survival rate for the first year was 50 per cent, while the 5-year and 10-year survival rates were 20 and 12 per cent, respectively.

The basic data for the average curve in figure 2 are presented in table 10 so as to demonstrate how this and the other curves in this graph were prepared.

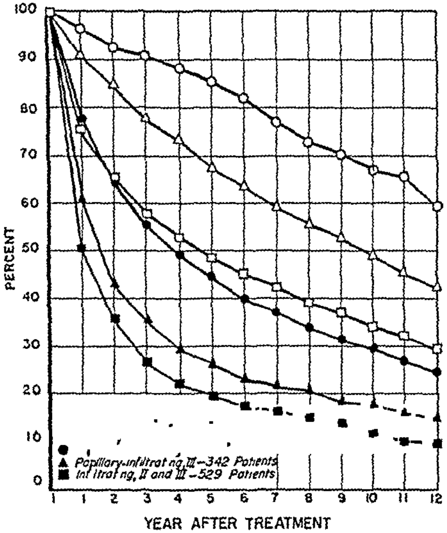

FIG 2 Initial carcinoma of bladder Survival rates after treatment

TABLE 10 *Calculation of survival rates by the actuarial method for 2615* patients with initial carcinoma of the bladder*

Interval Following Treatment (1)	Last Report		Total Persons Living at Beginning of Interval (4)	Person Years Exposed (5)	Probability of Dying in Interval (6)	Survival Rate at Beginning of Interval (7)
	Dead (2)	Living (3)				
years						*per cent*
0 to 1	621	70	2615	2580.0	0.2407	100
1 to 2	271	65	1921	1891.5	0.1448	76
2 to 3	172	60	1585	1555.0	0.1106	65
3 to 4	108	45	1353	1330.5	0.0812	58
4 to 5	90	59	1200	1170.5	0.0769	53
5 to 6	71	86	1051	1008.0	0.0704	49
6 to 7	63	88	894	850.0	0.0741	46
7 to 8	49	43	743	721.5	0.0679	42
8 to 9	36	60	651	621.0	0.0580	39
9 to 10	33	54	555	528.0	0.0625	37
10 to 11	33	64	468	436.0	0.0757	35
11 to 12	28	55	371	343.5	0.0815	32
12 and over	69	219	288	—	—	30

* Excludes 63 patients with no stated time interval

The method employed was the actuarial rather than the direct.[3] In the actuarial method the first column gives the interval in years from the designated time, which in this calculation is the time immediately after the first treatment. Columns 2 and 3 show the number of patients dead and alive, respectively, when last heard from, and column 4, the number of persons living at the beginning of the first specified period following initial treatment. Column 5, "person-years exposed", is obtained by subtracting from the persons living at the beginning of this period (i.e., column 4) half the number who were known to be alive at the last follow-up but who were lost in the interval (i.e., column 3).[3] Column 6, "the probability of dying in the interval" is obtained by dividing the figures in column 2 by those in column 5 (621/2580). The probability is found to be 0.2407. Translating this into percentage, of the 100 alive at the beginning of the study, 0.2407 (24.1 per cent) will die in the interval 1–2 years. This comprises the data in column 7 and constitutes the first year survival rate. The survival rates for successive years are obtained by repeating the same procedure step by step. It must be realized that the figures in column 7 are based on those in column 5 (i.e., person-years exposed) rather than on figures in column 4 (total living at the beginning of the period). This method is considered to give a better estimate statistically than the direct method.

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[3] BERKSON, J AND GAGE R P Calculation of survival rates for cancer Proc Staff Meet, Mayo Clin, 25: 270-286, 1950

When the survival rates of patients with noninfiltrating carcinoma were compared with those of patients with infiltrating carcinoma, it was found that the rates for 1077 patients with noninfiltrating carcinoma were 92 per cent for one year, 73 per cent for 5 years and 54 per cent for 10 years, while the corresponding rates for 1,538 patients with infiltrating carcinoma were 64, 31 and 20 per cent, respectively. The 12-year survival rate for patients with noninfiltrating carcinoma was three times that for patients with infiltrating carcinoma (table 11).

Comparison of the survival rates with regard to the sex of patients showed

TABLE 11. *Comparison of survival rates of noninfiltrating (papillary) with infiltrating initial carcinoma of the bladder*

Interval Following Treatment	Survival Rate at Beginning of Interval	
	Type of carcinoma	
	Noninfiltrating carcinoma	Infiltrating carcinoma
years		
0 to 1	100.	100.
1 to 2	92.	64.
2 to 3	87.	48.
3 to 4	81.	40.
4 to 5	78.	34.
5 to 6	73.	31.
6 to 7	69.	28.
7 to 8	64.	25.
8 to 9	60.	23.
9 to 10	58.	21.
10 to 11	54.	20.
11 to 12	51.	18.
12 and over	47.	16.
Number with data*	1077	1538

* Excludes 63 patients with no stated time interval.

that although women with noninfiltrating carcinoma were, on an average, 3 years older than men (see table 1), yet the survival rates for both sexes were approximately the same during the first 7 years after treatment For infiltrating carcinoma, it will be recalled from that table that the average age of women was 61 years as compared to 60 years for men, nevertheless, the survival rates were definitely more favorable for women than for men (fig 3) Survival rates for

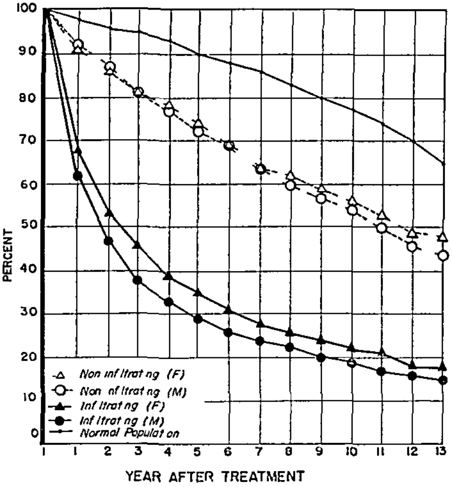

FIG 3 Survival rates of male and female patients with noninfiltrating and infiltrating initial carcinoma of bladder

TABLE 12 *Comparison of survival rates for various age groups of patients with noninfiltrating initial carcinoma of the bladder*

Interval Following Treatment	Survival Rate at Beginning of Interval			
	Age groups			
	40–49	50–59	60–69	0–9
Years				
0 to 1	100	100	100	100
1 to 2	95	95	84	78
2 to 3	93	90	73	68
3 to 4	91	85	63	58
4 to 5	90	81	57	52
5 to 6	89	76	48	42
6 to 7	85	74	43	38
7 to 8	81	69	36	30
8 to 9	77	67	28	24
9 to 10	75	64	26	20
10 and over	72	60	21	19
Number with data	177	392	173	119

TABLE 13. *Comparison of survival rates for various age groups of patients with infiltrating initial carcinoma of the bladder*

Interval Following Treatment	Survival Rate at Beginning of Interval			
	Age groups			
	40–49	50–59	60–69	70–79
Years				
0 to 1	100.	100.	100.	100.
1 to 2	69.	67.	63.	57.
2 to 3	51.	52.	47.	42.
3 to 4	44.	42.	38.	34.
4 to 5	38.	37.	33.	28.
5 to 6	34.	33.	30.	25.
6 to 7	32.	31.	27.	20.
7 to 8	31.	27.	25.	16.
8 to 9	30.	25.	23.	14.
9 to 10	27.	23.	21.	12.
10 and over	26.	22.	20.	10.
Number with data	207	520	626	330

both white men and white women[4] in a normal population are also shown in figure 3.

Comparison of survival rates for various age groups showed that in patients with noninfiltrating carcinoma the 1-year survival rate for 40–49, 50–59, 60–69, 70–79 year groups were 95, 95, 84 and 78 per cent respectively; the corresponding 5-year rates were 89, 76, 48 and 42 per cent, and the corresponding 10-year rates were 72, 60, 21 and 19 per cent (table 12). For patients with infiltrating carcinoma the survival rates for the same age groups were 69, 67, 63 and 57 per cent respectively for 1 year; 34, 33, 30 and 25 per cent for 5 years; 26, 22, 20 and 10 per cent for 10 years (table 13). Whereas the 10-year survival rates for patients in the 60–69 year group were the same regardless of whether the patients had noninfiltrating or infiltrating carcinoma, the rates for patients with noninfiltrating carcinoma were twice as high in the 70–79 year group and three times as high in the 40–49 and 50–59 year groups as for those with infiltrating carcinoma.

SUMMARY

Two thousand six hundred and seventy-eight patients were selected from the Bladder Tumor Registry for this study. These patients presented themselves for previously untreated carcinomas of the bladder; they had no demonstrable metastasis when first examined; they were treated for the tumor, and they were followed for at least 5 years after the initial therapy.

Seventy-one per cent of the patients had single tumors, almost equally divided between those that involved single areas and those that involved more than one area (table 4).

Forty-two per cent of the patients with noninfiltrating carcinomas (papillary, grades 1 and 2) were "tumor-free" 5 years or longer after initial therapy, as compared to 18 per cent of the patients with infiltrating carcinomas; the 10-year rates were 27 and 11, and the 15-year rates 13 and 6, respectively (tables 7, 8, and 9).

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[4] DUBLIN, I., LOKTA, A. J. AND SPIEGELMAN, M.: Length of Life. New York: The Ronald Press Co., 1949, pp. 12–15.

For the entire group, regardless of the grade of the tumor, the survival rates were 76 per cent for 1 year, 49 per cent for 5 years, and 35 per cent for 10 years. For patients with papillary carcinoma, grade 1, however, the 1-year survival rate was 96 per cent, the 5-year rate 85 per cent, and the 10-year rate 67 per cent, while corresponding rates for infiltrating carcinoma, grades 2 and 3, were 50 per cent, 20 per cent and 12 per cent. The 12-year survival rate for patients with noninfiltrating carcinoma was three times as great as for those with infiltrating carcinoma.

The survival rates of patients with infiltrating carcinoma were definitely more favorable for women than for men. Although the survival rates for various age groups were distinctly more favorable in patients with noninfiltrating than in patients with infiltrating carcinoma, the 10-year rates in the age group 60–69 were the same for both (figure 3 and tables 12 and 13).

The author wishes to express his appreciation to Drs. Archie L. Dean and William P. Herbst of the Registry Committee; Dr. Harold Dorn of N.I.H. and Dr. E. L. Hamilton of O.T.S.G. for critical review and suggestions; and to Mrs. Mardelle Clark Reynolds for advice on interpretation of statistical data.

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

A STUDY OF 2678 PATIENTS WITH INITIAL CARCINOMA OF THE BLADDER: II. SURVIVAL RATES IN RELATION TO THERAPY

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WITH THE STATISTICAL ASSISTANCE OF MARY S. LEVITIN AND JEAN H. GERENDE

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In a previous communication the survival rates of 2,678 patients with initial carcinoma of bladder were reported.[1] The present study attempts to compare the survival rates of patients treated by radon implantation with those treated by surgical methods* without radiation.

The patients selected for the study are the same patients who formed the basis for the study of survival rates.[1] The selection of the material, the diagnostic criteria and other pertinent information have been reported in the previous study.

Most of the cases were contributed by large teaching hospitals where it may be assumed that the patients were treated properly. It is known that for most patients the treatment was definitive rather than palliative; however, it must be clearly understood that none of the patients were seen or treated by the author, who had no decision in the choice of therapy, did not know why one form of treatment was preferred to the other, whether it was appropriate, adequate or uniform and what the immediate results of therapy were in terms of symptomatic relief. Another factor to be considered in this, as in many reports on the treatment of bladder tumors, is that many patients received more than one form of therapy either concurrently or at different times. Nevertheless, this brief account of the observations seems to be justified, especially since it is not intended to advocate one form of therapy in preference to another or to draw any specific conclusions.

This presentation will deal with two aspects of the subject: 1) A within-rate comparison of survival and "tumor-free" rates of patients having various grades of carcinoma treated by radiation alone, "open surgery"† with or without radiation, and "closed surgery"‡ with or without radiation; 2) within-rate comparison of survival and "tumor-free" rates of patients having various grades of carcinoma treated by radiation alone with those treated by resection alone. Rates of both types are computed from time of first treatment.

It must be realized that since some tissue was removed from every patient, in those listed under radiation, tissue was excised for the purpose of histopatho-

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Accepted for publication July 29, 1955.

* Included under surgery were transurethral and segmental resection, excision and fulguration.

[1] Mostofi, F. K.: A study of 2678 patients with initial carcinoma of urinary bladder. I. Survival rates. J. Urol., 75: 480–491, 1956.

† Cystotomy.

‡ Operation performed by the transurethral approach, none of the patients in this group were treated by cystotomy.

logic examination and not as the therapeutic measure of choice. In this group radiation was considered the therapeutic measure. Less than half the patients grouped as radon cases were treated by closed radon alone, the remainder by open radon; but since the rates were only slightly different the 2 groups (closed and open radon) were combined under radon.

In contrast to this group are 1) those patients from whom as much of the tumor as could be excised surgically was removed, but the therapy was supplemented by radiation, and 2) those who were treated solely by surgical procedures without any radiation.

Seventy per cent of the group under open surgery had open surgery alone, 16 per cent had open surgery followed by transurethral procedures, 9 per cent had surgical procedures of both types at first hospitalization, and 5 per cent had closed followed by open surgery.

A. PATIENTS TREATED BY RADIATION COMPARED WITH THOSE TREATED BY OPEN AND BY CLOSED SURGERY

1. Survival rates (figures 1 to 5)

Papillary carcinoma, grade 1: Of the 317 patients in this group there were 12 who were treated by radon (1 open and 11 closed). Because the number was too small to give reliable results, survival rates were omitted from figure 1. Seven of these patients were dead: 2 less than one year; 1 one to two years; 1 three to four years; 1 six to seven years; 1 nine to ten years and 1 eleven to twelve years. Five were living: 1 five to six years; 1 six to seven years; and 3 twelve years or more. Fifty-seven patients were treated by open surgery without radiation with one, five and ten year survival rates of 98, 90 and 71 per cent respectively; 26 were treated by open surgery and radon with corresponding rates of 92, 76 and 50 per cent; 180 were treated by closed surgery alone with corresponding rates

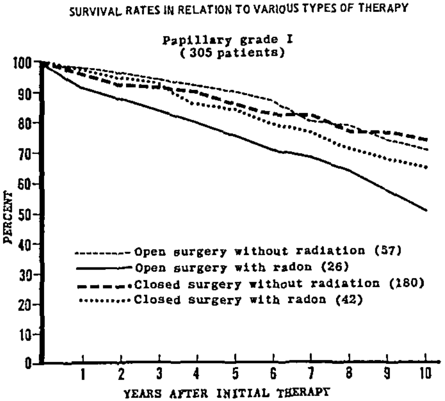

FIG. 1

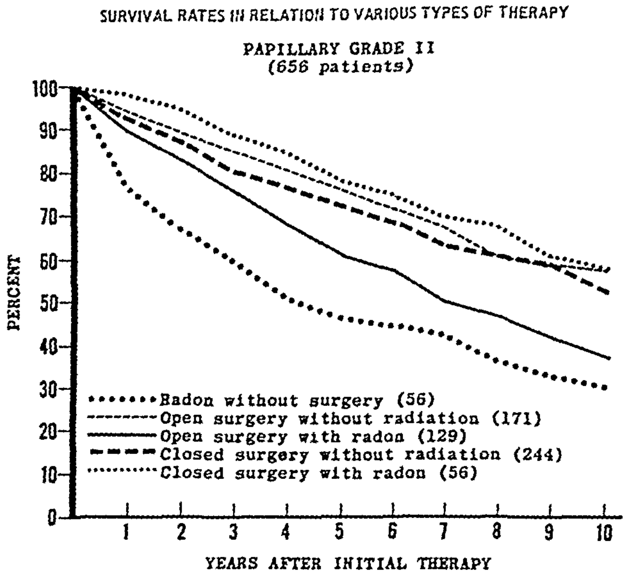

FIG. 2

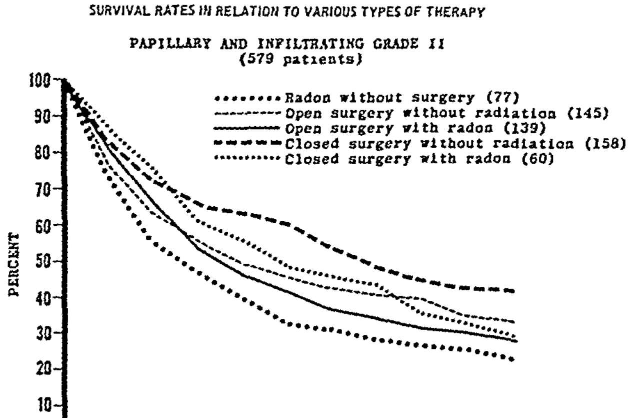

FIG. 3

of 97, 86 and 74 per cent; 42 were treated by closed surgery and radon with the corresponding rates of 98, 85 and 65 per cent.

Papillary carcinoma, grade 2: Among the 656 patients, 56 were treated by radon alone with one, five and ten year survival rates of 77, 47 and 31 per cent, respectively; 171 were treated by open surgery without radiation with corresponding rates of 94, 77 and 59 per cent; 129 were treated by open surgery and radon with corresponding rates of 90, 62 and 38 per cent. Two hundred and forty-four patients were treated by closed surgery alone with corresponding rates of 93, 73 and 53 per cent; 56 patients were treated by closed surgery and radon with corresponding rates of 98, 78 and 59 per cent.

Papillary and infiltrating carcinoma, grade 2: Of the 579 patients, 77 were treated by radon alone with one, five and ten-year survival rates of 71, 32 and 23 per cent, respectively; 145 were treated by open surgery without radiation

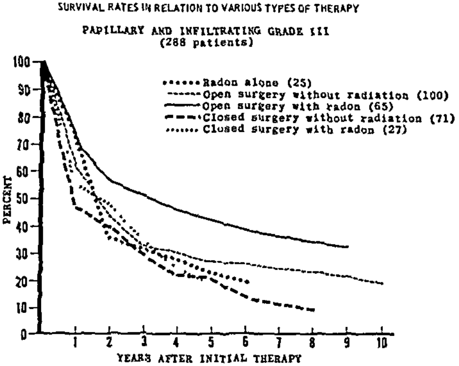

FIG. 4

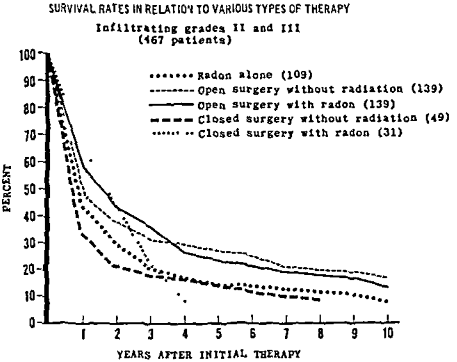

FIG 5

with the corresponding rates of 75, 45 and 32 per cent, 139 were treated by
surgery and radon with the corresponding rates of 79, 41 and 28 per cent,
were treated by closed surgery alone with the corresponding rates of 82, 60
41 per cent, 60 patients were treated by closed surgery and radon with
corresponding rates of 85, 48 and 29 per cent.

Papillary with infiltrating carcinoma, grade 3: Of the 288 patients, 25
treated by radon alone with one and five-year survival rates of 72 and 24
cent, respectively; 100 were treated by open surgery without radiation
corresponding rates of 62 and 28 per cent, 65 were treated by open surgery
radon with corresponding rates of 72 and 43 per cent; 71 patients were tre
by closed surgery alone with corresponding rates of 47 and 21 per cent, an
patients were treated by closed surgery and radon with corresponding rate
55 and 20 per cent

Infiltrating carcinoma, grades 2 and 3: Of the 467 patients, 109 were tre by radon alone with one, five and ten-year survival rates of 43, 15 and 9 per cent, respectively; 139 patients were treated by open surgery without radiation with the corresponding rates of 48, 27 and 17 per cent; 139 were treated by open surgery and radon with the corresponding rates of 58, 24 and 14 per cent; 49 patients were treated by closed surgery alone with one and five-year survival rates of 34 and 15 per cent, respectively and 31 patients were treated by closed surgery and radon with a one-year survival rate of 65 per cent and a four-year survival rate of 9 per cent.

Thus in patients with papillary and infiltrating carcinoma, grade 3, and infiltrating carcinoma, grades 2 and 3, the rates were generally better for those treated by open surgery and radon than by any other method. Patients with papillary carcinoma grade 1 treated by open surgery without radiation had better over-all survival rates than those treated by closed surgery with or without radon. In addition, although patients with papillary noninfiltrating carcinoma grade 2 treated by closed surgery with radon had the better survival rates, those patients treated by closed surgery without radon had lower survival rates than those treated by open surgery without radon.

2. Five-year "tumor-free" rates (figures 6 and 7)

Papillary carcinoma, grade 1: Of the 251 patients, 14 were treated by radon alone with a 5-year "tumor-free" rate of 50 per cent; 42 were treated by open surgery without radon with the corresponding rate of 48 per cent; 16 were treated

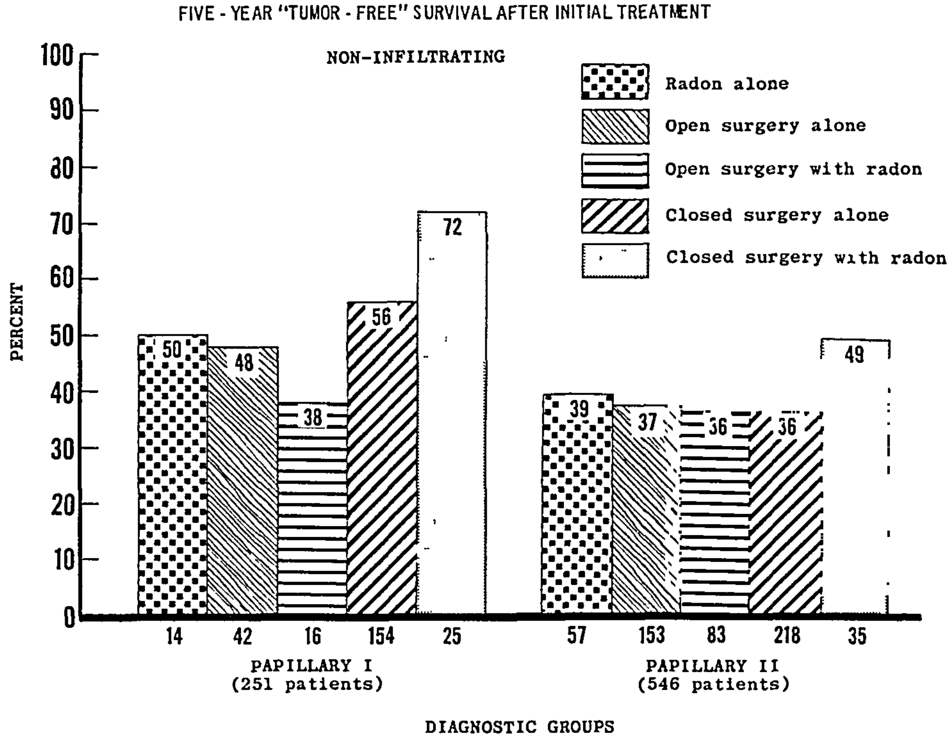

FIG. 6

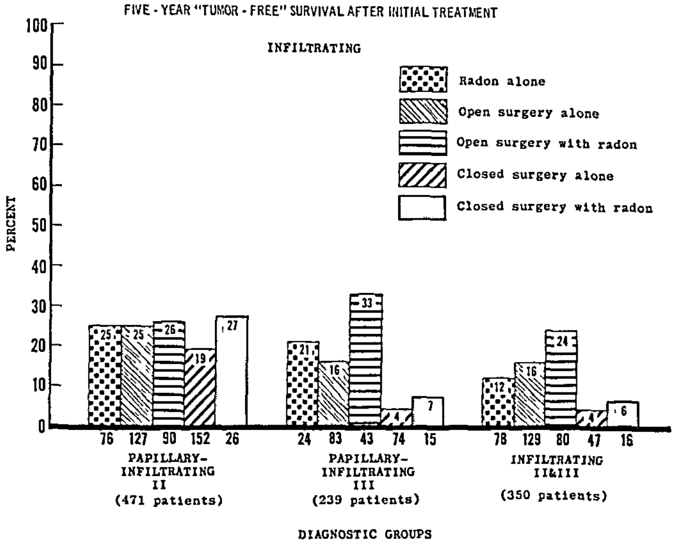

Fig. 7

by open surgery and radon with a corresponding rate of 38 per cent; 154 were treated by closed surgery only with the rate of 56 per cent, and 25 were treated by closed surgery and radon with the corresponding rate of 72 per cent.

Papillary carcinoma, grade 2: Of the 546 patients, 57 were treated by radon alone with a 5-year "tumor-free" rate of 39 per cent; 153 were treated by open surgery without radiation with a corresponding rate of 37 per cent; 83 were treated by open surgery and radon with the corresponding rate of 36 per cent; 218 were treated by closed surgery alone with the corresponding rate of 36 per cent; and 35 were treated by closed surgery with radon with a corresponding rate of 49 per cent.

Papillary and infiltrating carcinoma, grade 2: Of the 471 patients, 76 were treated by radon with the 5-year "tumor-free" rate of 25 per cent; 127 patients were treated by open surgery with the corresponding rate of 25 per cent; 90 patients were treated by open surgery and radon with the corresponding rate of 26 per cent; 152 patients were treated by closed surgery alone with the corresponding rate of 19 per cent and 26 were treated by closed surgery and radon with the rate of 27 per cent.

Papillary and infiltrating carcinoma, grade 3: Of the 239 patients, 24 were treated by radon alone with a 5-year "tumor-free" rate of 21 per cent; 83 were treated by open surgery without radiation with the corresponding rate of 16 per cent; 43 were treated by open surgery and radon with the corresponding rate of 33 per cent; 74 were treated by closed surgery without radiation with a 5-year "tumor-free" rate of 4 per cent and 15 were treated by closed surgery and radon with a corresponding rate of 7 per cent.

Infiltrating carcinoma, grades 2 and 3: Of the 350 patients, 78 were treated by radon alone with a 5-year "tumor-free" rate of 12 per cent; 129 were treated by open surgery without radiation with a corresponding rate of 16 per cent; 80 were treated by open surgery and radon with a 5-year "tumor-free" rate of 24 per cent; 47 were treated by closed surgery alone with a corresponding rate of 4 per cent, and 16 patients were treated by closed surgery and radon with a corresponding rate of 6 per cent.

Thus, while for patients with papillary and infiltrating carcinoma, grade 3, and infiltrating carcinoma, grades 2 and 3, higher 5-year "tumor-free" rates were observed in patients treated by open surgery and radiation, for noninfiltrating papillary carcinoma, grades 1 and 2, the rates were better for patients treated by closed surgery and radon.

B. RADON IMPLANTATION ALONE COMPARED TO SEGMENTAL RESECTION ALONE

1. *Survival rates* (*figure 8*)

Two hundred seventy-nine patients with initial carcinoma of bladder were treated with radon implantation alone (after biopsy) and 131 by segmental resection alone. Some of the patients initially treated by segmental resection had similar resection at a later date and some who were originally treated by radon had subsequent radon implantation, but none of the patients received more than one type of therapy.

Papillary carcinoma, grade 1: Six patients were treated by segmental resec-

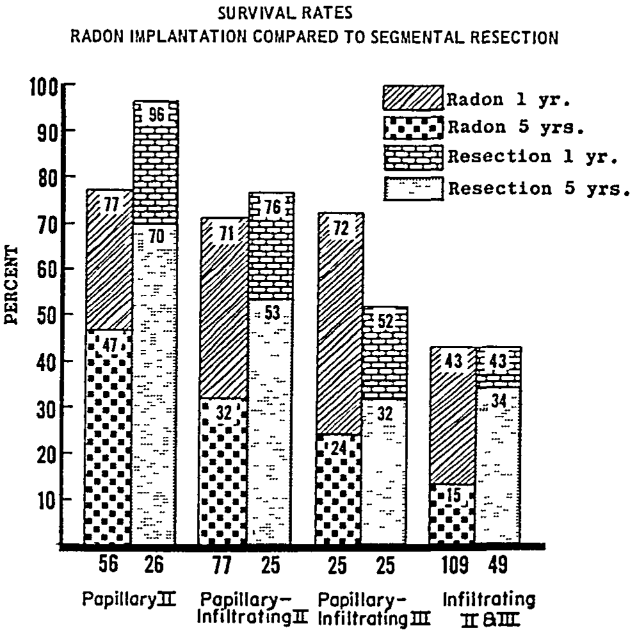
SURVIVAL RATES
RADON IMPLANTATION COMPARED TO SEGMENTAL RESECTION

FIG. 8

tion alone, all were alive at the end of the first year and 4 after five years. Twelve patients were treated by radon alone, 10 were alive at the end of one year and 8 after 5 years. As the number of patients treated by segmental resection or radon was too small to reach reliable conclusions, survival rates for papillary grade 1 were omitted from figure 3.

Papillary carcinoma, grade 2: For 56 patients treated by radon, the one and five-year survival rates were 77 and 47 per cent, respectively; for 26 patients treated by segmental resection alone the corresponding rates were 96 and 70 per cent.

Papillary and infiltrating carcinoma, grade 2: For 77 patients treated by radon the corresponding rates were 71 and 32 per cent respectively; for 25 patients treated by segmental resection alone the corresponding rates were 76 and 53 per cent.

Papillary and infiltrating carcinoma, grade 3: For 25 patients treated by radon alone, the one and five-year survival rates were 72 and 24 per cent respectively; for 25 patients treated by segmental resection alone the corresponding rates were 52 and 32 per cent.

Infiltrating carcinoma, grades 2 and 3: For 109 patients treated by radon alone, the corresponding rates were 43 and 15 per cent; and for 49 patients treated by segmental resection the corresponding rates were 43 and 34 per cent.

Thus in general the overall rates were better for patients treated by segmental resection alone than by radon implantation alone.

2. Five-year "tumor-free" rates (figure 9)

There were 249 patients who had a single radon implantation and 135 who had a single segmental resection. None of the patients had any other form of treatment for at least six years after the initial therapy.

Papillary carcinoma, grade 1: For 14 patients treated by radon, the 5-year

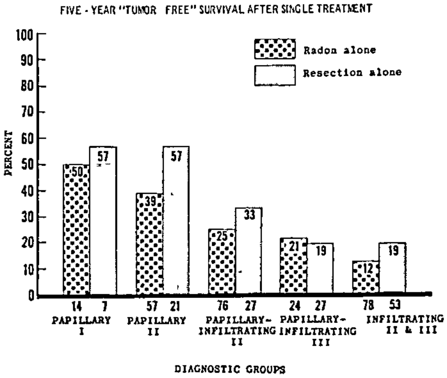

FIG. 9

"tumor-free" rate was 50 per cent; for 7 patients treated by resection alone the corresponding rate was 57 per cent.

Papillary carcinoma, grade 2: For 57 patients treated by radon the rate was 39 per cent; for 21 patients treated by segmental resection alone the rate was 57 per cent.

Papillary and infiltrating carcinoma, grade 2: For 76 patients treated by radon alone the rate was 25 per cent; for 27 patients treated by segmental resection, the rate was 33 per cent.

Papillary and infiltrating carcinoma, grade 3: For 24 patients treated by radon alone the rate was 21 per cent; for 27 patients treated by segmental resection the rate was 19 per cent.

Infiltrating carcinoma, grades 2 and 3: For 78 patients treated by radon alone, the rate was 12 per cent; for 53 patients treated by segmental resection the rate was 19 per cent.

Thus, on the whole, the rates were better for those treated by segmental resection than by radon implantation. It should be emphasized that the number in some of the categories is small.

SUMMARY

An effort has been made to compare the survival rates of patients with various types of carcinoma of bladder treated by radon with those treated by surgery. While patients treated surgically seemed to fare better on the whole than patients treated by radiation, caution is urged in the interpretation of the results as the numbers in each category are too small and the factors which led to the decision as to the type of therapy are unknown. The problem deserves comprehensive study.

The author wishes to express appreciation to Drs. Archie L. Dean and William P. Herbst of the Registry Committee; Dr. Harold Dorn of N.I.H. and Dr. E. L. Hamilton of O.T.S.G. for critical review and suggestions; and to Mrs. Mardelle Clark Reynolds for advice on interpretation of statistical data.

The Journal of Urology
Vol. 75, No. 3, March 1956
Printed in U.S.A.

A RADICAL OPERATION FOR THE CURE OF INTRACTABLE STRICTURE OF THE MALE URETHRA

ARTHUR B. CECIL

Surgeons have long hesitated to cut into the pendulous urethra for any purpose due to the great difficulty encountered in the past in closing fistulas of that portion of the urethra. Because of this, strictures of the pendulous urethra have heretofore been treated almost entirely by dilatation and by internal urethrotomy, even though these procedures offered no possibility of permanent cure.

I shall limit my discussion to an operation which I devised for the radical cure of intractable strictures of the pendulous urethra. Johanson has recently published an article on the surgical treatment of strictures of the pendulous and deep urethra. In the treatment of strictures of the pendulous urethra Johanson divided the strictured portion of the urethra on its ventral surface, and sutured the skin to the edges of the divided strictured urethra. The urethra was later constructed by the second method of Duplay. The work of Johanson in transplanting skin of the scrotum to deeper portions of the urethra, and the excision methods as practised by Hamilton Russell and others for the cure of strictures of the deeper portions of the urethra, in my opinion will require more study. Thus, the transplantation of hair-bearing skin from the scrotum to form a part of the deep urethra will as certainly create urethral calculi as it did in the Bucknall operation.

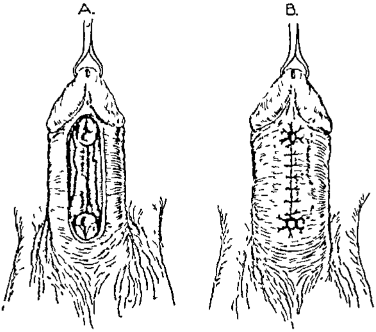

Fig. 1. *A*, strictured penile urethra has been excised. *B*, proximal and distal ends of urethra are sutured to skin edges, and skin closed along ventral surface.

In 1936 I described an operation for the construction of the urethra in hypospadias, and in 1946 I published an article in which I applied the technique of this operation to the cure of fistulas of the pendulous portion of the urethra, and stated that this operation would cure defects of the urethra no matter of what degree. It then occurred to me that, in intractable strictures of the pendulous

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Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif May 23–25, 1955.

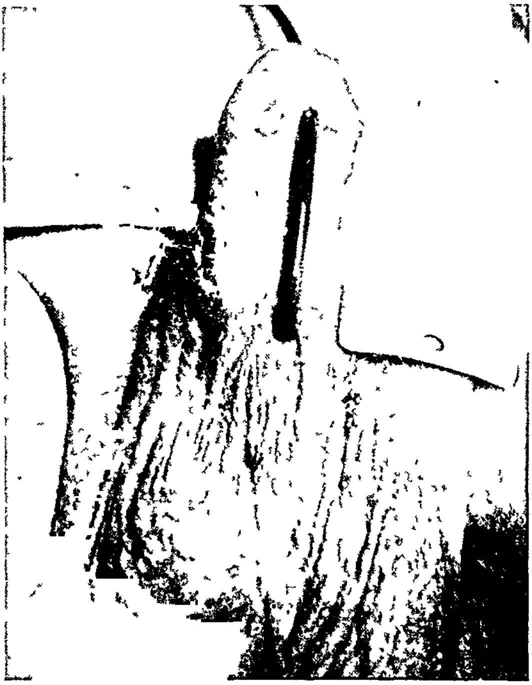

FIG. 2. Bougie has been introduced through meatus and into proximal urethra showing that urethra has been excised for 3 inches.

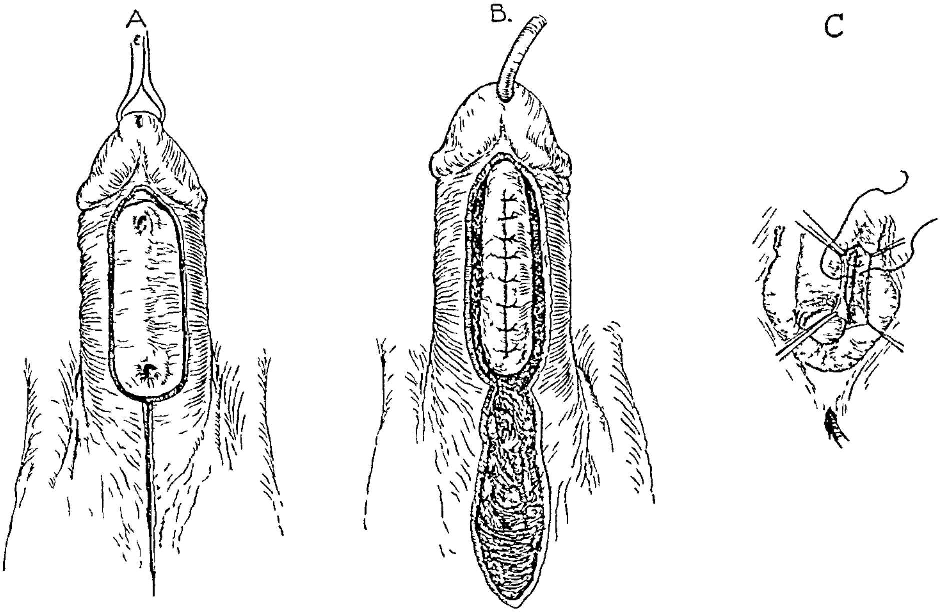

FIG. 3. *A*, incision made through skin to construct urethra over catheter, an incision has been carried down midline of scrotum for distance equal to penile incision *B*, urethra has been constructed over catheter; tissues have been dissected back on scrotum *C*, penis sutured down to scrotum using continuous 000 catgut suture Skin of penis is then sutured to skin of scrotum with interrupted dermal sutures.

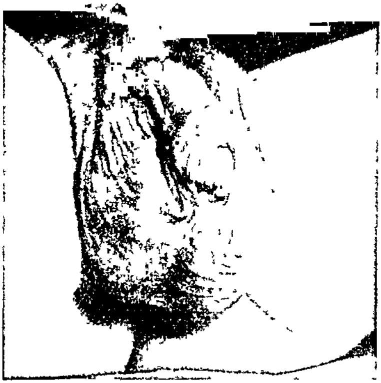

Fig 4 Postoperative result of suturing penis to scrotum

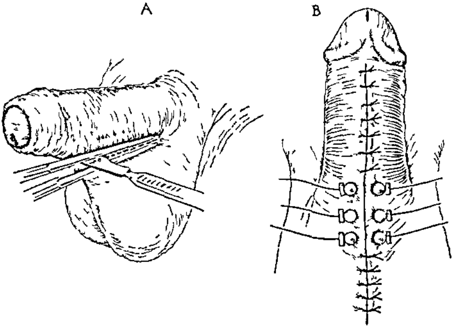

Fig. 5. *A*, two clamps are placed between scrotum and penis, penis cut free from scrotum. *B*, penile and scrotal incisions are closed. *At penoscrotal angle, double lock sutures are used.*

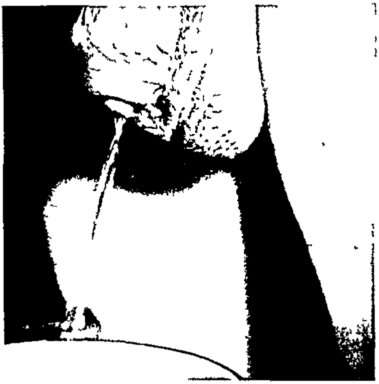

Fig 6. Postoperative result showing cure of stricture of urethra, large size urinary stream, good force. No postoperative dilatation has been necessary.

urethra, there would be no difficulty in replacing the entire portion of a strictured urethra after excising it. Accordingly, I devised the operation which I wish to demonstrate today, the steps of which are shown in figures 1 to 5. The postoperative result is shown in figure 6.

CONCLUSIONS

In the future, all strictures of the urethra that require prolonged dilatation should be treated by radical surgical methods. A study should be made as to the best method of dealing with strictures of the deeper portions of the urethra. The operation which I have described offers a perfect cure for all strictures of the pendulous urethra.

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The Journal of Urology
Vol 75 No 3 March 1956
Printed in U S A

CARCINOMA OF THE MALE AND FEMALE URETHRA PATHOLOGY AND DIAGNOSIS

ARCHIE L DEAN

CARCINOMA OF THE MALE URETHRA

Pathology The epithelium lining the male urethra is composed of many layers of cells Proximally it closely resembles the transitional epithelium of the bladder with which it is continuous at the internal urethral orifice Throughout the cavernous portion of the canal, the lining cells are columnar while distally, in the fossa navicularis, they become flat Although the great majority of urethral cancers in men arise from columnar epithelium in the cavernous urethra, with few exceptions, the neoplasms are composed of squamous cells This is probably the result of chronic irritation bringing about squamous metaplasia and malignant degeneration

Urethral tumors are commonly classified according to their place of origin but since the anatomical divisions of cavernous, membranous and prostatic urethra are inconsistent with clinical experience, the presently accepted clinical divisions of the urethra for tumor location are penile, bulbomembranous and prostatic, respectively Primary tumors of the prostatic urethra are exceedingly rare A majority of the growths develop in the bulbomembranous urethra and involve the perineum Since approximately 20 per cent of the tumors of the penile urethra arise in the fossa navicularis from external virus infections or as the result of congenital meatal strictures and since these growths can be treated more conservatively and have a definitely better prognosis, the clinical problem is simplified by classifying them separately

Etiology Between 1926 and 1954, 59 patients with urethral cancers were examined and treated at the Memorial Hospital Of these patients, 46 were women and 13 were men, a ratio of nearly 4 to 1 The average age of men when the urethral cancer is discovered is said to be about 55 years and the age of greatest incidence about 60 years The average age of the Memorial Hospital patients at admission was 64 years While predominantly a disease of the elderly, it has been reported in a youth of 18 years

The great majority of urethral cancers arise apparently from the effects of chronic irritation In rare instances no contributing cause can be found About 75 per cent of the patients suffered from chronic urethral irritation produced by recognized strictures, infections or trauma The frequent association of urethral strictures and subsequent cancers at the stricture site has long been recognized While the majority of observers have found about 50 per cent of urethral cancers superimposed on strictures, an incidence as high as 76 per cent has been reported Strictures from straddle injuries are followed by urethral cancers with especial frequency, possibly because they are composed of so much contracting scar tissue that they produce tight stenoses and perhaps because the mucosa of the bulbo-

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Read at annual meeting, American Association of Genito Urinary Surgeons, Pebble Beach Calif May 23-25, 1955 membranous urethra when chronically irritated more readily undergoes malignant degeneration.

Gonococcal infections, which in the past gave rise to a large proportion of precancerous strictures, seldom have been described as so closely preceding discovery of a tumor as to be a precipitating cause. On the other hand, mixed infections, largely maintained by strictures, probably play a considerable part in producing long-standing urethral irritation. Their frequency and virulence are demonstrated by the common occurrence of periurethral abscesses as stricture complications.

The trauma usually mentioned in the etiology of urethral cancers is produced by the passage of sounds. I doubt its importance. At any rate, when sounds are necessary, most, if not all, of the other causative agents have been present for some time. However, there is often a close time relationship between the use of sounds and discovery of a tumor.

The most common tumor of the penile urethra is the delicate papilloma which usually arises from the distal 2 cm. of the fossa navicularis. These benign growths are said to result from virus infections. In a number of tumors of the urethral meatus, with no other influence apparent, it has appeared reasonable to ascribe considerable etiological importance to the repeated trauma of the urinary stream impinging on the mucosal rim of the stenosed meatus. The effects of such irritation in the penile or bulbomembranous urethras have not been recognized.

Except for the unusual direct extension of a bladder tumor along transitional epithelium to the posterior urethra, no urethral cancers have been described as possibly resulting from the chronic irritation of cancerigenic substances in the urine. This is noteworthy since tumors of the ureter and the bladder follow tumors of the kidney pelvis so regularly as to be expected. The rarity of urethral cancers in patients with pre-existing tumors of transitional epithelium suggests that the mucosa of the urethra may be more resistant to chronic irritation from cancerigens in the urine or that the urine remains in contact with urethral mucosa for too short a time to initiate changes. However, the fact that tumors in an otherwise normal urethra may occur in patients with no evidence of disease in the upper urinary tract could be interpreted as evidence that urethral mucosa may be extraordinarily sensitive to irritants in the urine. Possibly the rapid and forceful passage of urine containing crystals may subject the normal urethra to a form of irritation absent in the upper urinary tract. Such possibly far fetched speculation appears permissible because it is likely that all of the influences producing urethral cancers are, as yet, unknown.

After years of chronic urethral irritation, usually from obvious causes but occasionally without any preceding disease, the cancer begins to grow. It expands and infiltrates, destroying the urethra in its progress and invading the periurethral tissues and the corpora cavernosa.

The literature repeatedly contains the statement that urethral cancers remain localized for a long time. It is true that as a group squamous cancers do not metastasize as early in their development as certain other tumors but the length of time a specific neoplasm remains localized is difficult to measure because one rarely knows just when malignancy first appears. This information in the urethra is seldom apparent The clinician soon learns to place no dependence on a urethral tumor to remain localized after experience shows the frequent presence of metastases when the tumor is first recognized

The male urethra is richly supplied with lymphatics Those from the penile urethra drain into deep subinguinal nodes which communicate with external iliac nodes Lymphatics from the bulbomembranous urethra communicate with external iliac and pubogluteal nodes, while those of the prostatic urethra unite with the other lymph vessels of the prostate and drain into a cephalad group of external iliac nodes It is evident, therefore, that lymph borne metastases from urethral tumors are likely to be inaccessible to clinical investigation unless exposed surgically After tumors grow from the urethra into the cavernous tissues, widespread dissemination through the bloodstream may occur

Symptoms There are no precancerous symptoms or characteristic early symptoms of urethral cancers in men For a considerable time the clinical picture is that of stricture When the tumor produces symptoms, it is well advanced Pain during erections is one of the earliest symptoms and a sticking, burning pain during urination soon ensues Following ulceration of the growth, a serosanguinous urethral discharge having the offensive odor of necrosis is likely to develop

A cancer must be suspected when the patient reports that his accustomed treatment with sounds was followed by unusually active bleeding which continued for a longer time or that his stricture closed unusually soon following dilatation Not infrequently, closure of the urethra is complete Sometimes spontaneously, more often after the passage of sounds, a painful, inflamed, indurated area may appear in the periurethral tissues external to the stricture If this is incised to drain a periurethral abscess, grumous material rather than pus may be evacuated and a rapidly growing, fungating tumor develops around a fistula Before this event, or soon afterward, if the growth is in the penile urethra, subinguinal nodes may become palpable

When a urethral tumor is not preceded by a stricture, the earliest symptom may be a spontaneous blood-tinged urethral discharge After such a growth becomes obstructive, dilatation is likely to cause unusually active bleeding because the constriction is produced entirely by delicate and highly vascular tissue

Tumors which arise in the fossa navicularis are usually discovered by the patient himself He is often led to examine the canal by observing that his urinary stream has become slower or that it has assumed an unusual shape Tumors which arise at the edges of the meatus appear at first as insignificantly small sores They grow slowly but steadily in spite of treatment with home remedies

See figures 1 to 4

Diagnosis In the writer's experience, the diagnosis of urethral tumors in men is usually easy because, with few exceptions, at the time of examination the disease is far advanced Such self evident diagnoses, however, are of little more than academic interest because, with the exception of tumors of the meatus and fossa navicularis, practically all of these patients are incurable On the other hand, the discovery of urethral cancers sufficiently early for treatment with a fair chance of a cure is exceedingly difficult and it seldom has been accomplished

Each patient with urethral obstruction must be examined with lively aware-

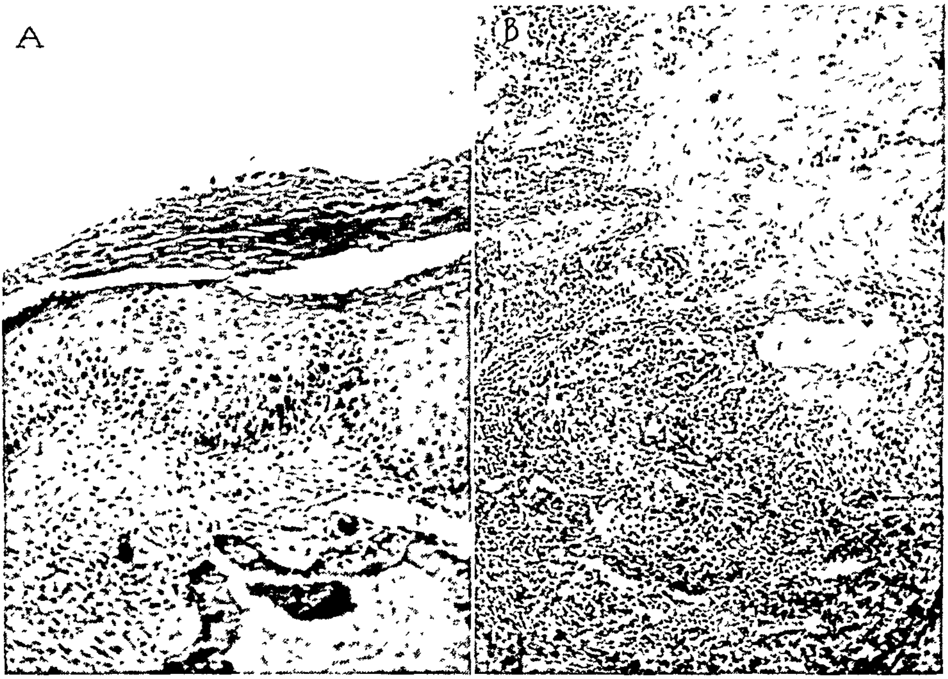

FIG. 1. *A*, epidermoid carcinoma of urethra, grade 3. *B*, metastasis in lymph node from primary tumor shown in *A*.

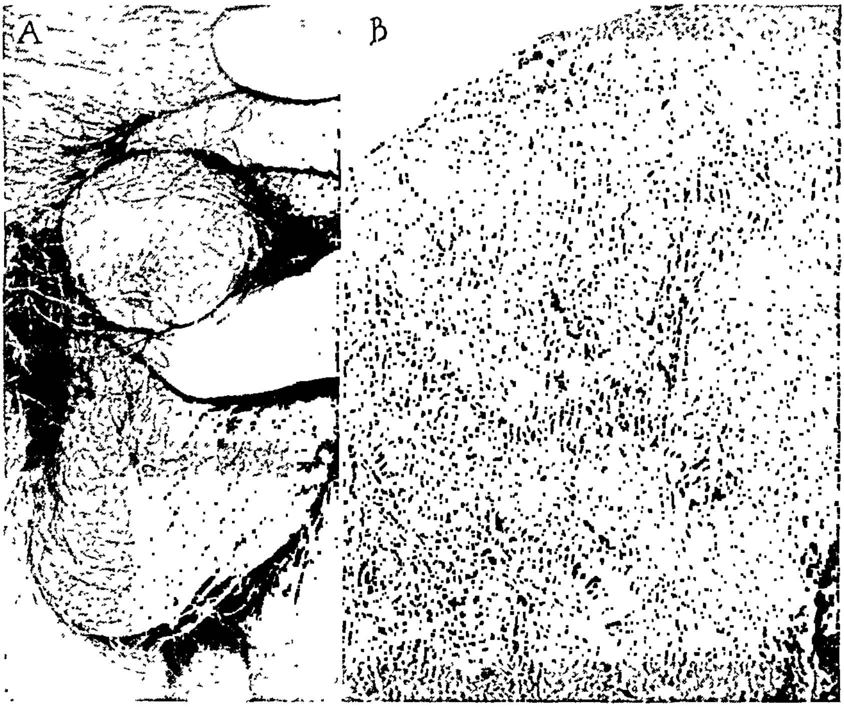

FIG. 2. *A*, primary carcinoma at urethral meatus. Patient observed this small sore growing gradually for 6 months. *B*, innocent appearing lesion shown in *A* proved to be squamous carcinoma, grade 3, as shown in figure 1, *A*.

ness that he may have a cancer. This is essential not only because early recognition of the tumor requires that special tests be performed but also because one must avoid certain common measures which could aggravate the disease

The diagnosis of a urethral cancer must be established by microscopic examination of material from the growth. Biopsies from fungating periurethral lesions need not be discussed but in order to prevent such disasters, investigation of periurethral induration must be made from within the canal. I know of no successes with cytological examinations and doubt whether urethral tumors are generally suitable for such investigations. Since most tumors begin to grow proximal to strictures, the endoscope seldom approaches them close enough to provide a clear view. For the same reason, urethrograms are usually unsatisfactory and, for the most part, show only the stricture. On the other hand, tumors growing independently of strictures can be visualized and adequate specimens can be removed from them with a cystoscopic rongeur. No instrument has been devised especially for performing biopsies on urethral tumors but the writer has found a ring curette of approximately 3 mm. diameter quite satisfactory for reaching the tumors and obtaining scrapings which may be embedded in paraffin and sectioned. About 90 per cent of the tumors prove to be squamous cancers while 10 per cent are papillary or transitional cell tumors or adenocarcinomas. Two women in the Memorial Hospital group had primary melanomas of the urethra but similar growths were not found in men.

The presence of metastases also should be established by microscopic examinations whenever possible. If the tumor originates in the penile urethra, failure to detect adenopathy in subinguinal nodes or failure to find microscopic evidence of cancer in enlarged nodes is good evidence but not positive proof that the disease is localized. Cancers in the bulbomembranous and prostatic urethras probably have metastasized by the time of their discovery, whether or not such extensions can be found. Excretory urograms may show pressure on the bladder or displacement of the lower ureter but only if metastatic pelvic nodes have become greatly enlarged. Careful surgical scrutiny of the external and internal iliac

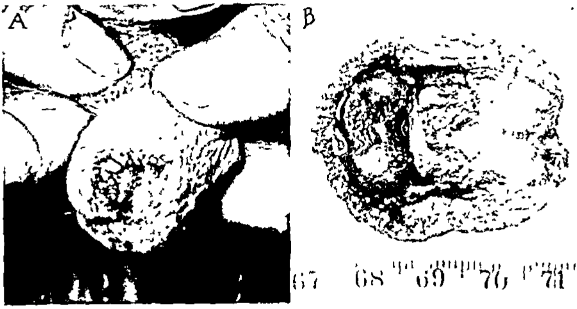

Fig. 3. *A*, primary tumor at urethral meatus involving glans. *B*, showing origin near meatus of tumor depicted in *A*.

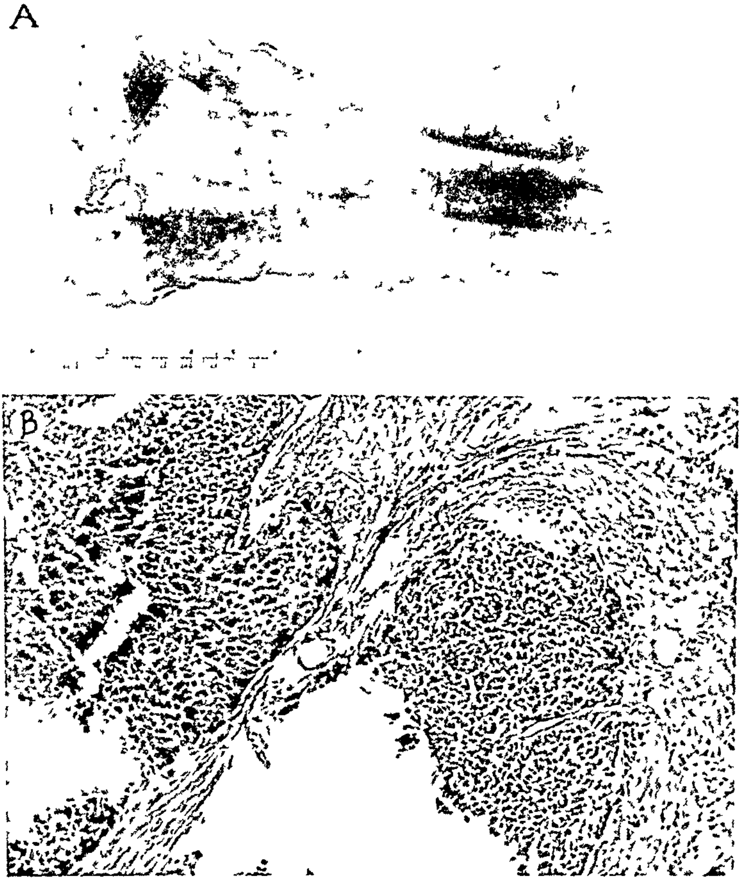

Fig. 4. *A*, carcinoma of penile urethra with no preceding stricture or other recognizable source of chronic irritation. *B*, photomicrograph of gross specimen shown in *A*

lymphatics probably is the most accurate way to show extensions of the disease through lymphatics but here, as with bladder tumors, there is likely to be at least a 10 per cent factor of error due to metastases which are inaccessible or occult. Finally, roentgenograms of the chest should be made in a search of blood-borne metastases.

If superficial tumors of a low grade of malignancy have spread from the bladder to the prostatic urethra, it is probable that, when found, the disease is confined to these organs. Infiltrating bladder tumors spread to the prostatic urethra much less frequently but at the time of their discovery, metastasis is likely.

CARCINOMA OF THE FEMALE URETHRA

The female urethra is a canal 2.5 to 4.0 cm. in length. It represents only the proximal portion of the male urethra. The posterior wall, except in its most proximal portion, is intimately connected with the anterior wall of the vagina. The external orifice lies between the labia minora. Local expansion and infiltration of a urethral cancer, therefore, invade these structures early with production of the usual vulvourethral tumor The epithelium lining the canal, in its proximal portion, is transitional in type, continuous with that of the bladder, distally it becomes squamous. This junction of columnar and stratified squamous epithelium, like that of the lip and anus, constitutes an area peculiarly subject to malignant degeneration The submucosa of the wall of the urethra is highly vascular. It is also richly supplied with lymphatics. These have terminations similar to those of the membranous and prostatic portions of the male urethra, passing to relatively inaccessible hypogastric nodes, to the medial suprafemoral nodes of the external iliac group and to the uppermost nodes of the external iliac group The lymph vessels of the urethrovaginal region and labia minora anastomose and pass to the superficial subinguinal nodes Involvement of these readily palpable nodes in the female, therefore, is evidence of considerable local tumor spread and probable involvement of nodes in the pelvis, whereas in carcinoma of the penile urethra, it usually indicates the earliest metastasis

See figure 5.

Etiology. The average age of women at the time of discovery of a urethral tumor is said to be about 52 years, in the Memorial Hospital group it was 57 While there may be great differences in age between the youngest and the oldest patients (in this series they were 35 and 75 years, respectively), the majority of the women were well beyond the menopause. Practically all were or had been married, the great majority, but not all, had had children. The past histories of women with urethral cancers showed no unusual features nor, previous to the onset of symptoms, were there significant references to the genitourinary tract.

As in men, urethral cancers in women have been attributed to chronic irritation and there is no reason to minimize the importance of this agent However, in women, it is likely to be more difficult to recognize the causes of chronic irritation which in a given patient produces a urethral cancer Possible causes are numerous, such as gonococcal and luetic infections and lymphogranuloma venereum

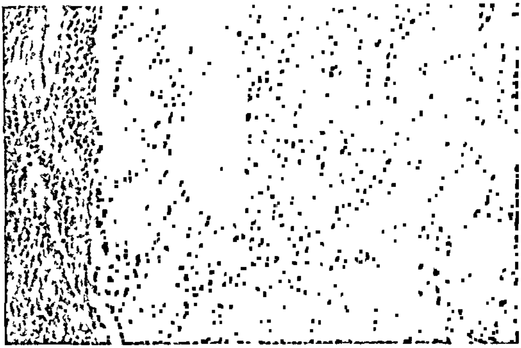

Fig 5 Primary melanoma of female urethra

Each of these may induce stenosis of the canal which further augments irritation. Mixed infections in congenital or acquired diverticula also are potent sources of both subacute and chronic urethritis. Birth injuries may leave changes such as strictures or eversion of the urethral mucosa which are recognized sources of chronic irritation and have been known to precede cancers. Bladder tumors in women seldom extend spontaneously into the urethra. Furthermore, urethral tumors in women rarely have been observed in individuals who have had tumors of transitional epithelium in the kidney, the ureter, or the bladder which could be attributed to the chronic irritation of cancerigens in the urine.

After a period of years during which the urethra has been subjected to the various types of irritation mentioned and perhaps also to other influences as yet unrecognized, a cancer or some other manifestation of chronic irritation may appear. The most common of the noncancerous changes are granular urethritis and productive lesions such as caruncles, papillomas and polyps. Recognition of any of these conditions calls for their prompt eradication and correction of the condition which produced them because their presence indicates that the factors which may produce a cancer have been in operation for some time.

In studying the etiology of urethral cancers in women, one is struck by the frequency of definite manifestations of chronic urethral irritation and the scarcity of urethral cancers and by the number of established urethral cancers in patients who described no previous urethral complaints.

Symptoms. Women may experience many symptoms from urethral cancers but hardly any occur before the growth is well established. There may be frequency, nocturia, urgency and intermittent, burning, terminal dysuria. Later there is likely to be dyspareunia, intermittent blood-tinged discharge, a slowing of the urinary stream, gradually increasing incontinence and finally greatly increased urinary difficulties, pain in the lower abdomen and complete retention. When the sequence of symptoms was clear, complete retention occurred about six months after the onset of frequency and nocturia. While individuals may seek relief from any of these symptoms, an unfortunately large proportion of patients were first examined when in complete retention. An occasional patient visited a physician after discovering a mass in the vulva and others some time after finding enlarging inguinal nodes.

Diagnosis. When discovered, urethral cancers in women usually appear as dark red productive lesions growing from the urethral meatus. There may be an exuberance of tissue to form a rosette 1 cm. or more in width. On the other hand, the meatus may be only slightly pink and swollen or a growth may protrude from within the canal while its rim is apparently uninvolved. The labia minora may appear distorted by contractures without abnormal changes in color or they may be destroyed by the spreading ulcer. Palpation shows more accurately the nature of the disease and its extent. The urethra usually is densely indurated and the common vulvourethral involvement can be felt radiating from the urethra for varying distances. Vaginal examinations usually are painful and the orifice may be stenosed. A relaxing anesthesia, therefore, and a rectal approach may be necessary when examining the pelvis for enlarged nodes. Subinguinal lymph odes usually are enlarged; to determine whether or not they are cancerous requires special investigation.

Endoscopic examinations are feasible with cancers of the female urethra although a traumatizing preliminary dilatation often is necessary. An ulcerating growth usually is seen and perhaps palpation against the instrument may outline the lesion more clearly. The most encouraging picture shows the growth limited to the distal urethra and thus possibly amenable to successful treatment. It is interesting to note that hypertrophy of the bladder musculature sufficient to produce trabeculation has been a common finding. Excretion urograms frequently show ureteral obstruction.

The diagnosis of cancer of the female urethra must always be established by the microscopic examination of adequate tissue from the lesion. As in the male, the great majority prove to be squamous cancers. Tumors of grades 2 and 3 predominate and different grades of malignancy may be represented in different portions of the same growth. A small proportion are papillary tumors, adenocarcinomas, polypoid tumors or mucoid tumors. Two patients in the Memorial Hospital series had primary melanomas. The true nature of inguinal adenopathy also should be proved histologically although extensive metastatic disease may exist deep in the pelvis without demonstrable involvement in the groins.

Among other important reasons for accepting only the positive biopsy as evidence of a urethral cancer is the difficulty of differentiating the neoplasm from productive lesions by clinical means. This is especially true of the urethral caruncle which is a benign vascular tumor which usually grows from the posterior wall of the urethra near the meatus. Caruncles may produce a burning pain, painful urination and bleeding. Caruncles do not invade the vulva nor do they infiltrate the wall of the urethra. Nevertheless, without a biopsy caruncles may be mistaken for cancers, cancers may be mistaken for caruncles, or cancers and caruncles may coexist with the malignant lesion masked by the benign.

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The Journal of Urology
Vol 75, No 3, March 1956
Printed in U.S.A.

THE TREATMENT OF URETHRAL TUMORS

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The treatment of urethral tumors will vary according to the sex of the patient, the location of the tumor, the local extent of the tumor, histological type of the tumor, and the presence or absence of metastases which may travel not only along the lymphatics, but also along the blood channels (fig. 1). Since primary cancer of the urethra, in both the male and female, is rare, and presents many variations, both in histology, location, and extent, generalizations with regard to therapy are difficult and individualization of therapy is necessary (table 1).

A study of the majority of the reported cases of male urethral tumors indicates that the armamentarium used for therapy has been 1) surgical excision or destruction of the tumor; 2) local application of some form of irradiation; 3) treatment of the lymph nodes; 4) palliative therapy. It has also very definitely shown that the problems posed and the results obtained are definitely related to the location of the tumor. Tumors arising in that portion of the urethra distal to the bulbous portion have apparently been recognized earlier, have posed less problems of therapy and yielded significantly better results than those arising in the bulbous, membranous or prostatic urethra (table 2).

From a review of the reported cases it would seem that about a third of th carcinomas of the urethra arise in that portion of the urethra which is distal t the bulbous portion. Surgical removal or destruction is the treatment of choic when the tumor is present in this locale. Of the 65 collected cases reported b Kreutzmann and Colloff,[1] 35 were cured. The type of therapy in these 35 is outlined in table 3. It will be noted that surgical removal of the involved area eithe alone or in conjunction with irradiation and removal of the regional lymph node was carried out in 33 of the 35. Radiation alone was used in 2 of the 35. In instances the regional lymph nodes were removed in addition to local removal the tumor. In one instance radiation of the regional lymph nodes was carrie out, and in two instances local radiation plus surgical excision was carried ou locally. Emasculation has been described as part of the surgical therapy in tum of the anterior urethra. It is rarely indicated except with extensive local involv ment of the skin and scrotum, and the probabilities are that when this is nece sary, the tumor is inoperable. In Hotchkiss'[2] report of 5 cases involving th portion of the urethra, the results of local surgical removal were poor. It probable because of his report of the high incidence of lymph node involveme that surgical therapy was applied relatively late in the course of the disease.

Only 2 cases of tumor involving the penile urethra were seen in the Universit Hospitals in the 20-year period between 1935 and 1955. Both of these presente

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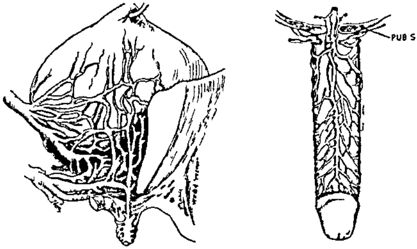
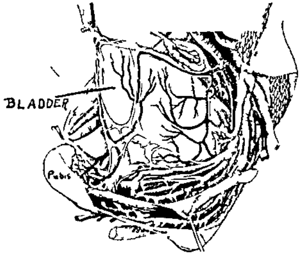
Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebbl Beach, Calif. May 23–25, 1955.

[1] Kreutzmann, H. A. R. and Colloff, B.: Primary carcinoma of the male urethra. Arc Surg., **39:** 513–529, 1939.

[2] Hotchkiss, R. S. and Amelar, R. A.: Primary carcinoma of the male urethra. J. Urol **72:** 1181, 1954.



VENOUS DRAINAGE – FEMALE URETHRA VENOUS DRAINAGE FROM PENIS



VENOUS DRAINAGE – MALE URETHRA

FIG 1 Note profuse venous drainage from urethra in both sexes

TABLE 1 *Tumors of the urethra Factors influencing therapy*

I Local extent —Breakdown of continuity of urethra especially as evidenced by abscess formation, infection, local rapid extension in new fascial plane
II Histological malignancy
III Location
  a) Penile urethra
  b) Bulbous urethra
  c) Membranous and prostatic urethra
IV Metastasis
  a) Lymphogenous
  b) Hematogenous
V Other findings
  Due to local disease
  Due to general disease

papillary tumors which responded well to destruction by coagulation No other treatment was carried out and the results were good, cures being obtained See figure 2

It would seem therefore that the basic therapy of tumors involving the penile urethra is surgical destruction In most instances, because of a possibility of invasion of the corpora cavernosa, partial or radical penile amputation with the construction of a perineal urethrostomy is indicated Local irradiation has rarely

TABLE 2. *Treatment of carcinoma of the urethra*

1. Surgical removal
2. Coagulation after exposure
3. Management of the lymphatics
    a) *Embolic phenomenon (Willis)*
    b) Anatomical considerations
        1) The network continuous with prostate and bladder
        b) The presymphyseal nodes
        3) The inguinal nodes
        4) The pelvic nodes
    c) Retrograde and irregular spread—possibility of blockage by infection reaction
    d) Surgical removal
    e) Radiation therapy
4. Local destruction by radiation therapy
    Radium needles, radon seeds, radium pack, isotopes
5. Palliative

TABLE 3. *Tumors of the penile urethra (collected series, Kreutzmann and Colloff 1939)*

Total 65; recovered, 35

Treatment in the 35 that recovered:	
Radical amputation + adenectomy	8
Extirpation of urethra + adenectomy	1
Amputation alone	20
Extirpation of urethra alone	1
Radiation alone	2
Amputation + radiation	2
Extirpation of urethra + x-ray to glands	1

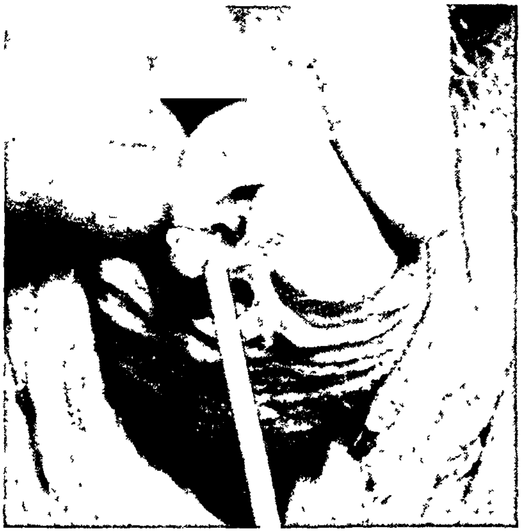


FIG. 2. Case of papillary tumor of penile urethra successfully treated by destruction with coagulating current.

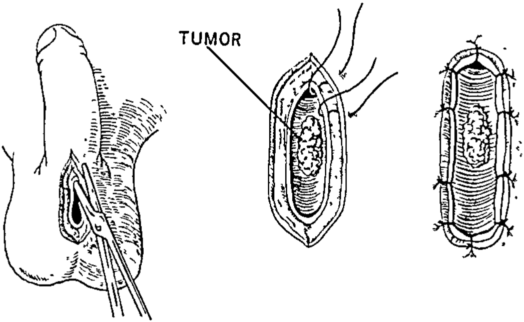


FIG. 3. Exposure of penile urethra for coagulation treatment of superficial tumor. Closure after several months of observation may be carried out by Johanson technique.

FIG. 4. Note bridge of skin which can be utilized to construct new urethra. Young's technique effects direct anastomosis between membranous and penile urethra.

been used and upon logical grounds is not so sure of destroying the lesion as surgery or cautery. The latter can be performed extensively through a temporary urethrostomy with later reconstruction of the urethra by a modification of the technique of Johanson[3] for extensive stricture of the urethra (fig. 3).

Tumors involving the bulbous, membranous and prostatic portion of the urethra make up at least two-thirds of the primary cancers of the male urethra. A small portion of these, however, do not extend posteriorly to any great extent and involve mostly the more distal portion of the bulbous urethra. These may be considered separately and are almost as accessible to surgical therapy as the tumors in the more distal portion of the urethra. The operation described by

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[3] Johanson, B.: Reconstruction of the male urethra in strictures. Acta Chir. Scandinav., Supp. 176, 1953.

TABLE 4. *Carcinoma of male urethra: University of Iowa Hospitals, 1935–1955*

No.	Case	Location	Treatment	Result
1	J. G.	Anterior	Coagulation	"Cured"
2	K. J.	Anterior	Coagulation	"Cured"
3	M. C.	Prostatic	Coagulation	Death
4	S. H.	Bulbous perineal extravasation	3000 R-irradiation S.P. cystostomy	Death
5	J. P.	Bulbous perineal extravasation	Radical with colostomy; nodes not involved	Died postoperatively
6	W. W.	Bulbous	Local excision	"Cured"

TABLE 5. *Tumors of bulbous, membranous, and prostatic urethra (collected series, Kreutzmann and Colloff 1939)*
Total, 77 cases; 9 recovered

Treatment in the 9 that recovered:	
Emasculation + adenectomy	1
Amputation + adenectomy	1
Amputation + adenectomy + x-ray	1
Excision of urethra + adenectomy	1
Amputation—radical	1
Resection of urethra + cystostomy	1
Amputation of penis + cystostomy	1
Resection of urethra + x-ray to glands	1
Excision of growth + local radium	1

Young[4] consisting essentially of a dissection of the bulbous urethra and the adjacent corpora with anastomosis of the distal anterior urethra to the membranous urethra is an example of the type of operative procedure which can be carried out in the smaller lesions located in this area. Essentially the same type of operative procedure was performed in the one case involving the distal portion of the bulbous urethra which occurred in our series (fig. 4). In this case resection of the urethra was accomplished leaving a perineal urethrostomy and a bridge of skin which could be used later for reconstruction of the urethra should the patient so desire (table 4).

When the more proximal portion of the bulbous urethra is involved or the membranous portion is involved, much more radical local procedure is necessary if a satisfactory excision of the local lesion is to be accomplished (table 5). Lesions involving the membranous urethra almost invariably extend through the urethral wall and will necessitate extensive removal of the bulbous urethra, the entire membranous urethra and the surrounding structures involving the superficial and deep layers of the triangular ligament and the structures between them. An operative procedure such as described by Uhle[5] or Goodwin[6] is indi-

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[4] Young, H. H.: A new radical operation for carcinoma of the bulbous urethra. Surg., Gynec. & Obst., **68:** 77–86, 1939

[5] Uhle, C. W. and Holfelner, E. D.: Treatment of carcinoma of male urethra by radical surgical infrapubic removal J. Urol , **68:** 302, 1952.

[6] Kaufman, J. J. and Goodwin, W. E.: Carcinoma of the male urethra: One stage surgical treatment by radical perineal excision and rectal transplantation of the divided trigone. Surg , Gynec. & Obst , **97:** 627–632, 1953.

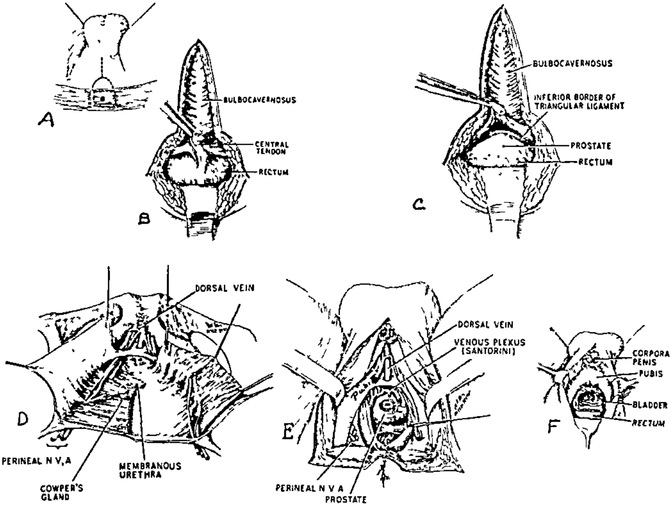

FIG. 5. Anatomical factors associated with removal of bulbomembranous urethra. *A*, perineal portion of incision. Note use of O'Conor shield for aid in localizing rectum. *B* and *C*, separation of rectum is carried out as for perineal prostatectomy. *D* and *E*, anatomical features of triangular ligament and its contents. These must be removed and bleeding controlled. *F*, appearance after such removal with prostate also removed. Remainder of bladder can be used for cystostomy drainage or can be removed from above when pelvic lymphatics are treated.

cated as far as the local removal of the tumor is concerned (fig. 5). Certainly coagulation through an external urethrotomy is of no avail, and in cases involving the prostatic urethra, local transurethral resection and coagulation except in very superficial tumors will not give satisfactory results. In one of our cases, the tumor arose primarily in the prostatic urethra and transurethral resection and coagulation of the tumor were carried out. No irradiation therapy followed this treatment, and it did not result in cure. It would seem that radical prostatectomy and urethrectomy with local removal of the regional lymph nodes would be the treatment of choice, and if such a radical procedure is not indicated, then *local transurethral coagulation with intraurethral irradiation of some type* should be done. Prostatectomy would not ordinarily suffice in these cases because the membranous urethra is usually involved, necessitating its removal together with the bulbous urethra in one mass. Diversion of the urine is effected by suprapubic cystostomy, cutaneous ureterostomy, or ureterocolostomy.

Radiation therapy for the local destruction of carcinoma of the male urethra has rarely been used. It was not used at all in any of our 6 cases. It was only used three times for tumors of the anterior urethra and four times for those cases involving the posterior urethra in the series collected by Kreutzmann and Colloff. In two of these it produced satisfactory local destruction of the tumor, but as I have indicated previously, logically it would seem that surgical removal can accomplish more and with greater certainty than local irradiation. Irradiation may be of value as an adjunct, however, in selected situations.

Before considering the management of the lymphatics, it is well to describe some points with regard to the lymphatic spread of cancer emphasized by Willis[7] in his studies of this subject. He states, "The spread of cancer cells by their growth as cords in the lumina of lymphatics is an unusual phenomenon in cases of operable cancer, and when it does occur the permeation is generally only of microscopic extent. In other words for operable cases of cancer, embolism is the only important type of lymphatic spread. Even in advanced cases with multiple glands affected, it is likely that embolism from gland to gland is largely responsible for the affected glands which may at first be discrete and unconnected. Later, however, adjacent glands become bound together by tumor-occluded lymphatics and infiltrated, extracapsular tissues." The second point which he makes is also of importance in consideration of the operability of the tumor: "Extensive lymphatic permeation is rarely or never a simple centrifugal process, but depends on confluence of separate zones of permeation from subsidiary foci in regional nodes established by metastases." These principles are useful in consideration of the type of operative procedure to perform with regard to the lymph nodes. Large masses of nodes mean retrograde lymphatic permeation and embolization with practical certainty of inoperability. On the other hand, local apparent operability may be associated with embolism to regional nodes which may satisfactorily be removed without block dissection to the original tumor. In other words, it would seem perfectly logical in instances involving cancer of these areas where local infection with infected regional lymph nodes may play a great part in confusing the issue with regard to involvement of the regional lymph nodes and in the repair of the wound following removal of these lymph nodes, to simply remove the tumor locally first and at a secondary stage after the local operative wound has healed to remove the regional lymph nodes.

The lymphatics[8] of the male urethra consist essentially of a lymphatic capillary network which extends throughout the entire length of the urethra developing from behind forwards. This is particularly abundant in the region of the fossa navicularis. These lymph vessels, according to Sappey, are united by multiple, transverse and oblique anastomoses. The network is continued posteriorly with that of the ejaculatory duct and the bladder, and anteriorly with that of the penis. This network empties into a group of collecting trunks which Poirier and Cuneo divide into four groups, those of the glans, those of the pendulous portion of the urethra, those of the bulbomembranous portion of the urethra, and the prostatic portion. Let us note before going ahead with the description of the various collecting trunks and the location of the regional lymph nodes that this capillary network may be the pathway for spread posteriorly from the more anterior portion of the urethra of tumor by local extension when collecting trunks leading to the inguinal nodes are blocked not only by tumor but also by

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[7] Willis, R. A.: Pathology of Tumours. St. Louis, Mo.: The C. V. Mosby Co, 1948.

[8] Tobias, M. J.: The Anatomy of the Human Lymphatic System. Ann Arbor, Mich.: Edwards Bros. Inc., 1938.

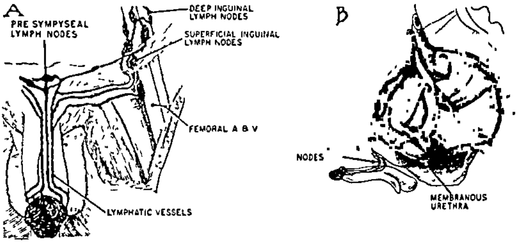
A
PRE SYMPYSEAL LYMPH NODES
DEEP INGUINAL LYMPH NODES
SUPERFICIAL INGUINAL LYMPH NODES
FEMORAL A & V
LYMPHATIC VESSELS
B
NODES
MEMBRANOUS URETHRA

FIG. 6. *A*, lymphatics of penile urethra. Note particularly presence of presymphyseal nodes. (After Testut.) *B*, lymphatics of bulbous and posterior urethra in male. Note extensive drainage to presacral nodes and nodes along external and internal iliac arteries.

the results of extensive infection. It then may well be that the tumor cannot spread by embolism to the regional nodes and must spread posteriorly, and therefore spread upward along the prostatic urethra, the base of the bladder and about the bladder into the pelvis.

The urethral collecting trunks in the region of the glans traverse the urethral wall on each side of the frenulum and are continuous with the collecting trunks of the glans which ascend along the prepuce to terminate with the latter. These form three or four dorsal collecting trunks which are carried backward (as illustrated in figure 6, *A*) under the fascia and along the deep dorsal vein towards the root of the penis. At the root of the penis they may terminate in a presymphyseal lymphatic plexus where there may be several intercalating nodules. From this plexus the lymphatics spread laterally to the region of the femoral canal emptying into the inguinal nodes.

The collecting trunks of the penile urethra appear on the inferior surface of the penis, soon around the corpora cavernosa and then travel with the collecting trunks of the glans terminating, as described above, in superficial inguinal, deep inguinal, femoral and even in the iliac nodes.

The collecting trunks of the bulbomembranous portion of the urethra may be divided into three groups of collecting vessels. One of these emerges from the superior surface of the bulbous portion of the urethra and follows the course of the urethral artery or the artery to the bulb and in this manner reaches the trunk of this blood vessel. The second collecting vessel ascends behind the symphysis pubis to terminate in the medial retrofemoral node. The third collecting vessel comes chiefly from the membranous portion of the urethra and is carried from below upward in front of the prostate and bladder and unites with the lymphatics from the inferior part of the anterior vesical wall, terminating in the retrofemoral and iliac lymph nodes. The lymphatics from the prostatic portion of the urethra are similar to those of the prostate and are illustrated in figure 6, *B*. It will be noted particularly that one group involving the apex of the prostate in the membranous urethra passes posteriorly to follow the vessels through Alcock's canal back to the hypogastric nodes.

Taking into consideration the underlying general principles of lymphatic metastases, as described by Willis and others, and the anatomical considerations of the lymphatic spread from the various portions of the urethra, as just reviewed, how are we to manage the problem of the lymphatics in these patients?

It is obvious, as emphasized by Hotchkiss, and also according to the studies of Willis, that a locally operable lesion may be completely removed surgically and yet have embolic involvement of the regional lymph nodes. In the anterior portion of the urethra involving primarily the pendulous, glandular and distal portions of the bulbous urethra, the lymphatic drainage for all practical purposes is primarily the nodes in the inguinal region and in the region of the femoral canal. Local surgical excision of the lesion, followed by block dissection of these regional lymph nodes on both sides, either at the same time as the original operative procedure is carried out, if very little infection is present, or as a secondary procedure following complete healing of the original lesion may be carried out in individual cases. It might be wise at the time that this procedure is carried out, to remove or at least study the iliac nodes lining the pelvis and the hypogastric nodes, since embolic involvement of some of these nodes may be present and they can readily be removed during the operative procedure (fig. 7).

If the original tumor involves the bulbous and membranous and prostatic portions of the urethra, exploration of the iliac and hypogastric nodes and their removal if involved are mandatory since more direct drainage to these areas is present in such cases, and they cannot be watched clinically.

When a good deal of local infiltration is present, usually associated with infection, irradiation therapy of the regional lymph nodes should be given serious consideration. It may also be of value in those instances where it is quite likely that no gross metastases are present, and it would seem that the radical lymph

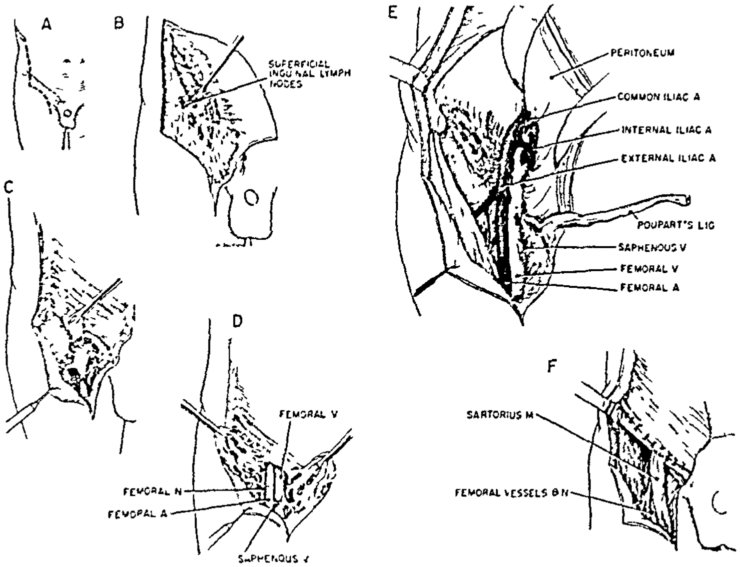

FIG. 7. Diagrams illustrating one type of surgical approach to inguinal and pelvic lymph nodes. Note disposition of inguinal ligament.

TABLE 6. *Carcinoma of the female urethra: Treatment and results by various authors*

Author	Treatment	No of Cases	No. of Cases Well
Fricke & McMillan	Radiation	24	7
Fricke & McMillan	Local excision + radiation	11	8
Sparks & Parsons	Various types	119	15
Taussig	Radiation	12	1
Taussig	Local excision + adenectomy	3	3
Taussig	Local excision alone	1	0
Auer	Local radiation + excision	14	6
Auer	Local radiation + excision + adenectomy	6	3
Kieth	Local radiation	3	3
Kaplan	Local radiation	2	1
Kaplan	Local radiation + local surgery	2	2
Kaplan	Local radiation + x-ray to nodes	1	0
Ritter	Radical surgery	9	5
Ritter	Radiation alone	11	0

TABLE 7. *Carcinoma of the female urethra: Recommended therapy by various authors (after Ritter*[9]*)*

Radical surgery locally and regional nodes .	10
Radium + local surgery or coagulation + x-ray to nodes .	10
Radium for primary + surgery to nodes	6
Local surgery and radium—nodes?	2
X-ray therapy to local and nodes	1
None satisfactory	2

node dissection would not be worthwhile; or in those instances where lymph node metastases are quite sure to be present and, for one reason or another, operative removal is not indicated. Hotchkiss has shown that these tumors are frequently fairly radiosensitive, and it may very well be that for all practical purposes, the metastases to the regional lymph nodes can be destroyed or their growth slowed down tremendously by intensive x-radiation. When one considers x-radiation it is important, as can be seen in figure 6, *A*, to give this therapy, not only to the inguinal nodes, but also the hypogastric and iliac nodes and also the nodes in the region of the symphysis itself.

There is some question as to the relative incidence of embolic phenomena and metastases to the regional lymph nodes. Hotchkiss feels that this is much more common than we are ordinarily given to believe. On the other hand, the results of the cases collected by Kreutzmann and Colloff would seem to indicate that *marked regional lymph node involvement comes on relatively late in the* course of the disease. However, for the most part, these cases come to us late and therefore serious consideration must be given to the regional lymph nodes and lymphatics.

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[9] Ritter, D. W.: Primary malignancy of the female urethra. West. J. Surg., **61:** 420–429, 1953.

TABLE 8. *Carcinoma of the female urethra: University of Iowa Hospitals, 1935–1955*

No.	Case	Treatment	Remarks	Result
1	E. M.	Local excision	Local recurrence treated with x-ray	Death
2	N. C.	Radium needles 2736 mg. hrs.	Local recurrence + metastasis	Death
3	J. C.	Local x-ray, 2000 R		"Cure"
4	N. H.	Local radium + x-ray treatment 2400 R		Death
5	B. H.	Local x-ray	Very extensive when seen	Death
6	R. K.	Local radium + x-ray	Very extensive when seen	Death
7	A. M.	Radon seeds + x-ray	No stricture, no incontinence	"Cure"
8	G. T.	Radium + 8000 R x-ray	Very extensive when admitted	Death
9	J. P.	Radium + x-ray	Very extensive when admitted	Death
10	L. A.	Local excision, coagulation, radium + x-ray, ureterointestinal anastomosis	Incontinence, lymph nodes not involved	"Cure"
11	B. R.	Local excision + coagulation	Incontinence	"Cure"

Carcinoma of the female urethra is a somewhat more common lesion than cancer of the male urethra. Moreover from the recorded experience its prognosis seems better than the corresponding lesion in the male which occurs in the bulbomembranous portion of the urethra. Also in contrast to the experience in the male, many more of these cases are treated by radiation therapy than by surgery (tables 6 and 7).

Fricke and McMillan[10] describe a group of 35 cases seen at the Mayo Clinic from 1918 to 1942. In 26 of these 35, enlarged inguinal nodes were present which means that the tumor has infiltrated the anterior vaginal wall. With radium alone, of the 35 cases, 14 were treated; two of these survived 5 years. Ten were treated with radium and x-ray therapy; five of these survived 5 years. Nine were treated with excision and radium; seven of these survived 5 years; and two were treated with excision, radium and deep x-ray therapy; one of these survived 5 years. The survival was approximately 28 per cent. E. W. Riches and T. H. Cullen[11] reviewed 28 cases. Ten of these were females and only one survived 5 years. They believe that distant metastases occur in one-third of all cases, and in 5 per cent metastases to the inguinal nodes are present.

In the 20-year period from 1935 to 1955, eleven cases of primary cancer of the female urethra were seen at the University Hospitals (table 8). The following forms of therapy were carried out: 1) local excision followed by deep x-ray therapy; 2) insertion of radium needles followed by deep x-ray therapy; 3) local

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[10] Fricke, R. E. and McMillan, J. T.: Radium therapy in carcinoma of the female urethra. Radiology, **52:** 533–540, 1949.

[11] Riches, E. W. and Cullen, T. H.: Carcinoma of the urethra. Brit. J. Urol., **23:** 209–221, 1951.

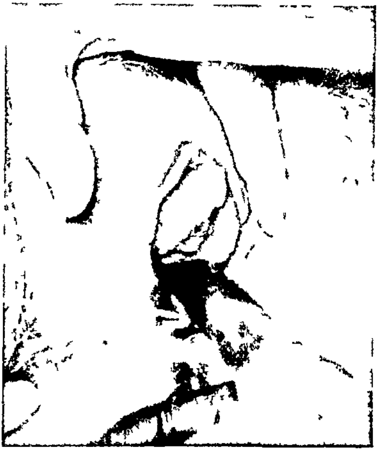

Fig 8 External appearance of case 1 of our female series An epidermoid carcinoma of urethra which appeared operable Surgical excision was tempered by attempt to maintain sphincter control Local recurrence and then widespread metastasis

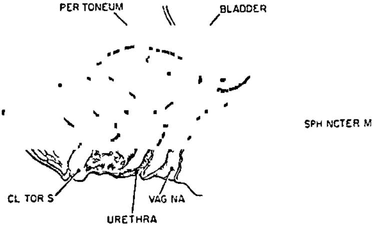

Fig 9 Female urethra Note location of sphincter musculature necessitating its sacrifice if radical destruction of tumor of any size in this location is to be achieved

x ray therapy alone, 4) radon seeds plus x ray therapy, 5) local excision by the use of a high frequency current followed by x ray therapy, 6) local excision and coagulation alone Of these 11 cases, four have apparently been cured of their tumors One had local destruction of the tumor by means of deep x-ray therapy alone Another had local destruction of the tumor with radon seeds and x ray therapy The third had local excision followed by radium and x ray therapy The fourth had local excision and coagulation alone Three of the four cases ended up with incontinence which was treated in one case by ureterointestinal anastomosis and in the other two by suprapubic cystostomy In this series of the seven who died of the disease, four had such extensive cancer at the time they first appeared for therapy that it was quite apparent no type of therapy would be more than palliative In the other three the lesions were apparently operable or apparently destructible. In one local excision was carried out which was not done widely enough because an attempt was made to save the sphincter. Local recurrence and spread of the lesion followed. It is likely that a more extensive local excision with diversion of the urinary stream might have led to a different outcome. In the other two irradiation was carried out rather than extensive local removal, again in the hope of saving sphincter control. In both local recurrence and metastases occurred (figs. 8 and 9).

From a review of our own cases, it would seem that the therapy for carcinoma of the urethra in the female falls essentially into the following situations. If the lesion is very small and distal to the sphincter, a combination of local excision or local radium or radon seed application with deep x-ray therapy to the regional lymph nodes offers a good chance for local destruction of the tumor and a cure. However, in the majority of instances, this type of lesion is not present and therapy should be essentially the same as that outlined for carcinoma of the male urethra involving primarily the bulbomembranous portion. In other words, wide excision of the local lesion, diversion of the urinary stream to take care of the incontinence, and management of the regional lymph nodes are indicated in much the same manner as outlined for those individuals with carcinoma of the male urethra.

Palliative therapy is of course of use only in those instances where curative therapy is no longer possible due either to distant metastases or to extensive involvement. Palliative therapy consists essentially of diversion of the urinary stream by means of ureterointestinal anastomosis, cutaneous ureterostomy, suprapubic cystostomy, small doses of deep x-ray therapy to relieve pain, chordotomy to relieve pain from spread and metastases and other palliative measures which might seem indicated in the individual instance. It is of necessity highly individualized depending upon the local problem. Its principles are the same for tumors occurring in either sex.

SUMMARY

In summary, then, the treatment of carcinoma of the male and female urethra is described on the basis of results of therapy in the literature, in six male cases and eleven female cases seen at the University Hospitals in the period 1935 to 1955, and the anatomical, pathological and surgical considerations involved.

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

THE EFFECT OF CORTISONE ON THE SPERMATOGENIC FUNCTION OF THE HUMAN TESTES

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Recent experimental evidence has shown that cortisone may influence spermatogenesis in the laboratory animal.

Cavallero, Rossi, and Borasi[1] found diminished testicular weight and a depression of spermatogenesis in rats treated with 1 mg. of cortisone acetate daily for 70 days followed by 5 mg. daily for 20 days. Antopol[2] found a decrease in testicular size and varying degrees of arrest of spermatogenesis in the mouse after the administration of cortisone.

Ingle,[3] and Winter, Silber, and Stoerk[4] found that 5 mg. and 3 mg. respectively of cortisone acetate daily did not produce a significant decrease in weight of the adult rat testes. Gaunt,[5] as well as Finerty,[6] found a relative, but not actual, increase in the weight of the rat testes after cortisone was given. They explain this as due to the lack of effect of the growth-inhibiting property of cortisone on the testes.

Sprague[7] has suggested that cortisone might have weak androgenic effects. He also feels that cortisone may cause a decrease in human libido.

Wilkins and Cara[8] used cortisone in the treatment of male children with congenital adrenal hyperplasia. They made a study of the testicular biopsies before and after therapy and noted that in those children above 7 years of age (bone age 13–14 years) there was an increase in spermatogenesis corresponding to that of the young adult. In the age group of 5 to 7 years (bone age 11 years), treatment caused a general maturation with some spermatid formation, and below 5 years of age (bone age 9–10½ years) little histological change was seen.

To determine the effect of cortisone upon spermatogenesis in adult man, a correlative study of seminal fluids and testicular biopsies has been carried out in a group of patients given this drug.

Read at annual meeting, American Association of Genito Urinary Surgeons, Pebble Beach, Calif., May 23–25, 1955.

[1] Cavallero, C., Rossi, L. and Borasi, M.: Studio sperimentale sugli effetti del cortisone, effetti morfologici sulle ghiandale endocrine del ratto. Sperimentale, 101: 226-235, 1951.

[2] Antopol, W.: Anatomic changes produced in mice treated with excessive doses of cortisone. Proc. Soc. Exper. Biol. & Med., 73: 262-265, 1950.

[3] Ingle, D. J.: The biologic properties of cortisone. A review. J. Clin. Endocrinol., 10: 1312-1354, 1950.

[4] Winter, C. A., Silber, R. H. and Stoerk, H. C.: Production of reversible hyperadrenocortinism in rats by prolonged administration of cortisone. Endocrinol., 47: 60-72, 1950.

[5] Gaunt, R., Tuthill, C. H., Antonchak, N. and Leathem, J. H.: Antagonists to cortisone. An ACTH like action of steroids. Endocrinol., 52: 407-423, 1953.

[6] Finerty, J. C.: Effect of hyper- and hypoadrenocortical function on young fat deficient male rats. J. Clin. Endocrinol. & Metab., 14: 823, 1954.

[7] Sprague, R. G., Power, M. H., Mason, H. L., Albert, A., Mathieson, D. R., Hench, P. S., Kendall, E. C., Slocumb, C. H. and Polley, H. F.: Observations on the physiologic effects of cortisone and ACTH in man. Arch. Int. Med., 85: 199-258, 1950.

[8] Wilkins, L. and Cara, J.: Further studies on the treatment of congenital adrenal hyperplasia with cortisone. V. Effects of cortisone therapy on testicular development. J. Clin. Endocrinol. & Metab., 14: 287-296, 1954.

MATERIALS AND METHODS

Four patients were selected from a large group with arthritic disease specifically requiring cortisone therapy. Because of the high incidence of oligospermia in this group, 7 patients with normal spermatozoa counts were selected from the urological department of a free clinic.

A complete general history and a specific sexual history were obtained. Each man had a complete physical examination. Special attention was given to the examination of the external genitalia and prostate. Routine laboratory studies were done on each patient as well as special urological examinations when indicated.

These men were in general good health except for minimal urological disease and the disease requiring treatment with cortisone. The age of the patients ranged from 33 to 74 years. The examination of the genitalia revealed the testes, in most instances, to be normal and the prostate to be enlarged by benign hyperplasia in three of the patients.

Semen specimens were obtained by masturbation in the laboratory after abstinence from sexual intercourse for at least 5 days. The specimens were collected in clean, wide-mouth glass containers. The analyses included observations on the volume, motility, numbers of spermatozoa (reported in millions per cubic centimeter), pH, and morphology. A minimum of three specimens were examined before treatment and at one to six week intervals during treatment.

Testicular biopsies were performed prior to treatment and during, or at the end of, therapy. The biopsies were unilateral and in the same organ when more than one biopsy was secured. The testicular tissue was obtained by incision and the material immediately fixed in freshly prepared Bouin's solution. The sections were stained with hematoxylin and eosin and Masson's trichrome technique.

The eleven men were given 75 mg. of oral cortisone* daily in three divided doses. In addition, 30 gr. potassium chloride were administered daily.

RESULTS

Seventy-five milligrams of cortisone were given daily over periods varying from 23 to 334 days. After 2 weeks' treatment, the cortisone was stopped in one patient because of hemorrhage in an unsuspected duodenal ulcer. No other complication of treatment was encountered.

Seminal fluid specimens prior to treatment revealed 2 of the patients to be oligospermic. One patient was unable to produce semen specimens.

The numbers of spermatozoa in the 10 patients securing specimens revealed the variabilities during treatment to be not significantly different from the variation before or after the drug was given. Similarly, there was no significant alteration in the sperm motility or normal morphology during treatment as compared to the specimens secured before and after treatment.

Testicular biopsy was performed on the 11 patients prior to therapy. Biopsies were also done on 6 patients during or at the end of the cortisone treatment. In these 6 patients, histological examination of the pretreatment and post-treatment biopsies revealed no significant change

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* The cortisone acetate (cortone) was supplied for this study through the generosity of Merck & Co., Inc., Rahway, N. J.

No history of alteration of libido could be elicited from the ten potent patients

CONCLUSIONS

Cortisone in amounts of 75 mg daily does not alter the spermatogenic function of the adult human testes

There is no significant difference between pretreatment spermatozoa counts and those obtained during and after treatment with cortisone

There is no alteration in spermatozoa motility or morphology produced by the treatment with cortisone

In 6 patients there was no significant change in the germinal cell elements as evidenced by histological examination of testicular biopsies before and after cortisone therapy

ADDENDUM

Maddock, Chase and Nelson (J Lab & Clin Med , **41:** 608–614, 1953) treated four adult men with large amounts of cortisone daily from 22 to 36 days, testicular biopsies secured before and after treatment showed little morphological change Studies of the seminal fluid in two of the men revealed an apparent decrease in the number of spermatozoa during and after treatment

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

DEPENDENT DRAINAGE VIA THE PERINEUM IN RETROPUBIC PROSTATECTOMY

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The operation of retropubic prostatectomy for benign prostatic hypertrophy has gained great popularity as it combines the complete enucleation of the obstructing tissue and the immediate excellent urinary control obtained by suprapubic prostatectomy with a minimum of postoperative hemorrhage and shock, and a much more comfortable postoperative course for the patient. However, in a small but significant percentage of cases this operation has been followed by osteitis pubis. This feared complication is serious on acccount of the prolonged incapacity and pain which it causes, and is a real potential drawback to the operation.

The prevesical space, also called the space of Retzius, or nowadays the retropubic space, becomes contaminated by urine, which is usually infected, in the course of various operations on the bladder and prostate by the abdominal route, including retropubic prostatectomy. On account of its dependent position and its tough watertight floor, formed by the endopelvic fascia and the prostatic capsule, its only avenue of drainage is upward between the undersurface of the symphysis pubis and the anterior wall of the bladder. Consequently, once it has been contaminated, its depth and its poor natural "up-hill" drainage tend to favor the pocketing of infected material and the spread of infection in the loose fatty tissue of this space. The development of such infection can be prevented by proper suprapubic drainage of this space, which is therefore considered by most operators to be essential whenever this area has been opened and contaminated.[1] Sometimes, when the drainage of this space is not adequate, infection results, and occasionally a frank abscess forms which extends by the path of least resistance upward behind the symphysis pubis to the suprapubic wound where drainage takes place.

Although opinions as to the etiology of osteitis pubis are not unanimous, the preponderance of evidence indicates that infection in the prevesical space plays an important role. Osteitis pubis was almost unknown before retropubic prostatectomy, and the great majority of cases have followed this operation.[2] In almost every case of osteitis two common denominators are present—a urinary infection exists, and the prevesical space has been opened. For practical purposes, in every instance of retropubic prostatectomy the prevesical space is exposed to possible infection through contamination with infected urine at the time of operation, and possibly later also, if leakage occurs through the suture line in the prostatic capsule. If the suprapubic drain is removed prematurely, such infection may be left undrained. It is well known that undrained urine, even

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Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23–25, 1955.

[1] Chute, R.: A note on drainage of the prevesical space. Trans. New Eng. Branch Amer. Urol. Assoc., 1938, pp. 5–8.

[2] Mortensen, H.: Osteitis pubis. J. Urol., 66: 412–417, 1951.

when it is sterile, is irritating to the tissues.[3] Also, it has been shown that oxidized cellulose and gelatin (oxycel and gelfoam), which sometimes have been used to control oozing in the prevesical space, are detrimental to wound healing, especially in the presence of infection to which they offer a favorable medium.[4] The same is true when necrotic tissue is left as a result of fulguration of bleeding vessels in or near the prostatic capsule. One or more of these circumstances just mentioned often occur following retropubic prostatectomy and favor the development of inflammation and infection which undoubtedly play a role in causing osteitis pubis. Lavalle and Hamm[5] produced important evidence in favor of an infectious etiology when they surgically biopsied the symphyses pubis of 3 patients with osteitis following retropubic prostatectomy and, using special culture methods, recovered Pseudomonas aeruginosa from all three biopsies, and in addition the Bacillus proteus in one of the cases. Microscopically the tissue showed subacute chronic inflammation involving periosteum, bone and cartilage. No suppuration was seen, but the process suggested infection of low virulence and long standing. Several nerves with advanced degenerative changes were seen. Kirz[6] also biopsied a case of osteitis following prostatectomy, and when he cut down to the bone found pus giving a scanty growth of Pseudomonas, the same organism which Lavalle and Hamm had found. On microscopic examination also much the same picture was seen, the soft tissue showing a chronic pyogenic infection, and the bone chronic inflammation. The pathologist in this case, T. C. H. Bemans, said: "It is a fair assumption that the inflammation of the pubic bone and the suppuration of the adjacent soft tissues are associated processes. Both are of a mild or subacute type, the organism found, i.e., Ps. pyocyanea (pseudomonas) is not uncommonly found in old-standing infections of the bladder . . ." The delay of several weeks before symptoms appear also suggests that a low grade infection, smouldering undrained in the loose fatty tissue of this space, very likely plays a part, perhaps by direct extension, perhaps by leading to thrombosis of the end vessels (arteries and/or veins) supplying the symphysis, which are small terminal branches from the obturator and inferior epigastric vessels. Also it is possible that interference with the nerve supply of these small vessels or to the periosteum and bone is a factor, and this could well be caused by such an infection and chronic inflammation, as was shown by Lavalle and Hamm's finding of nerves showing degeneration. No matter what the exact mechanism, infection is incriminated by the bulk of the evidence. That infection and inflammation may occur in the prevesical space without necessarily being accompanied by osteitis is evidenced by the unduly prolonged drainage from the wound which is sometimes seen following retropubic prostatectomy. Mr. Millin once told the senior author that he explained the well-recognized fact that osteitis pubis is exceedingly rare following radical retropubic prostatectomy on the basis that the operative procedure removes the prostatic capsule and endopelvic fascia which form the floor of the prevesical space, and thus provides free drainage away from the symphysis. Further evidence in favor of the undrained infection theory is that osteitis pubis is unknown following either conservative or radical perineal prostatectomy, where excellent dependent drainage always exists.

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[4] Hinman, F. Jr. and Babcock, K. O. Local reaction to oxidized cellulose and gelatin hemostatic agents in experimentally contaminated renal wounds. Surgery, 26: 633–640, 1949.

[5] Lavalle, L. L. and Hamm, F. C. Osteitis pubis. Its etiology and pathology. J. Urol., 66: 418–423, 1951.

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In view of the evidence that infection in the prevesical space is the important factor in the etiology of osteitis pubis, which has by far its greatest incidence following retropubic prostatectomy, and of the facts that this space is exposed to contamination and possible infection in almost every such prostatectomy, and that the natural drainage of this space is poor and "uphill", with a resulting propensity to infection, it seemed to the authors that dependent drainage of the prevesical space through the perineum would be more efficient than the customary suprapubic drainage, and therefore should be better prophylaxis against the development of infection there, and thus against the occurrence of osteitis pubis. This procedure has been carried out in 8 cases in recent months with satisfactory results, and forms the basis for this report.

Drainage of the prevesical space and the region of the prostate and bladder base via the perineum is not new. One of the authors has carried this out in a number of instances following cystectomy, having had this route pointed out to him many years ago by his father, the late Dr. Arthur Chute, who used it for drainage of infection around the bladder base, and published an article on it in 1924.[7] Fullerton of Belfast, Ireland, in 1929[8] and Silverton of Sydney, Australia in 1954,[9] both described perineal drainage of the bladder and prostatic cavity following suprapubic prostatectomy. Blocksom of Oklahoma, writing in the Mexican *Revista de Urologia*,[10] advocated drainage of the prevesical space following retropubic prostatectomy by a subpubic parapenile wick as prophylaxis against osteitis—and, of course, drainage of abscess of the prostate via the perineal approach was described by the late Hugh Young many years ago.[11] The technique which the authors have used is a composite of these various earlier procedures.

Before describing the details of the technique, it seems well to mention some of the anatomical features. Figure 1 is a diagram of the pelvis in sagittal section showing the good natural dependent drainage of the prevesical space afforded by perineal drainage contrasted to the less effective "uphill" drainage by the customary suprapubic wick. In figure 2, *A*, a sketch of the male perineum, the arrow shows the path of the drainage tract. From an inch-long incision in the perineum, slightly anterior to and to the left of the anus, and not far inside the

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[10] Blocksom, B. H.: Osteitis pubis. Revista de Urologia, **10:** 74–82, 1952.

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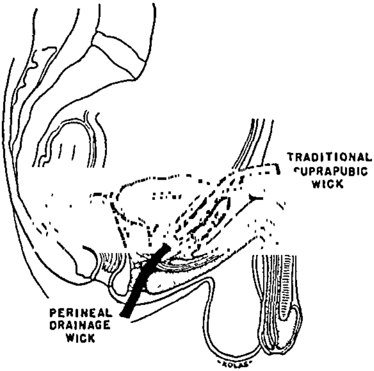

FIG. 1. Sagittal section of pelvis showing good dependent drainage of prevesical space through perineal wick contrasted with less effective "uphill" drainage from customary suprapubic wick.

pubic ramus, the dissecting finger passes just below the transversus perinei muscles (triangular ligament) and then goes upward through the left side of the upper *ischiorectal fossa—superficial to the levator ani muscle—to the left side* of the prostate where it pierces the endopelvic fascia, and thus enters the left side of the prevesical space through its floor. Figure 2, *B* is a diagram of a coronal section through the pelvis to include the bladder and prostate, and shows how the drainage tract goes through the left ischiorectal fossa, superficial to the levator ani muscle, and pierces the endopelvic fascia to enter the prevesical space at the left side of the prostate.

The operative technique is as follows: With the patient lying on his back, not only are the abdomen and external genitalia prepared but also the perineum, perianal region and the upper 12 inches of the inner aspect of the thighs. After the abdomen and perineum have been draped as one, assistants flex the knees and separate the thighs. *A one inch vertical incision is made in the perineum* slightly anterior to the anus and a little inside the left pubic ramus (fig. 3, *A*). The rather fibrous subcutaneous fat of the lower ischiorectal fossa is incised with scissors, and then the index finger of the right hand is introduced, passed easily under the lower edge of the transversus perinei muscles (triangular ligament), and then is directed upward through the upper left ischiorectal fossa in an easy plane of dissection which lies superficial to the levator ani muscle. At first the finger stays well to the lateral side of the fossa to avoid any possibility of injuring the rectum which lies in the midline. However, as the upper part of the fossa narrows, the finger comes easily and naturally to the left lateral lobe of the prostate (fig. 3, *B*). The dissection is easy, requires very little force, and is *not deep or confusing. If there is any question as to the location of the prostate*, this can easily be answered by passing a sound, by which the prostate can be moved somewhat and thus located. The finger is now withdrawn, and the

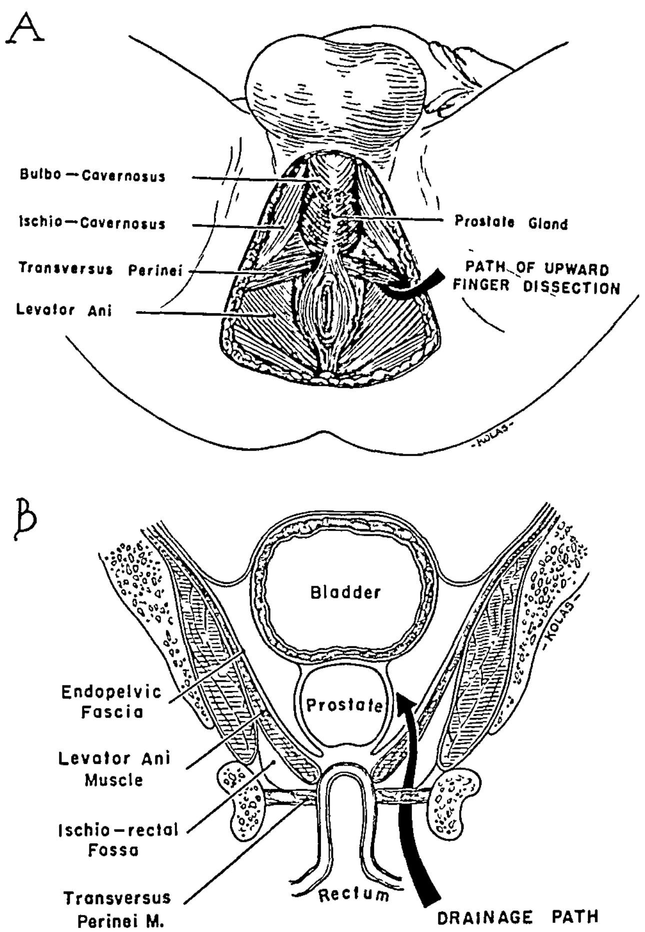

FIG. 2. *A*, diagram of perineal muscles. Arrow shows course of dissecting finger which enters perineum through small incision above and to left of anus, passes under transversus perinei muscle, then up left side of ischiorectal fossa, superficial to levator ani muscle, to left lobe of prostate. *B*, coronal section of pelvis. Arrow shows course of drainage tract which runs under transversus perinei muscle, and then up left side of ischiorectal fossa, superficial to levator ani muscle, to pierce endopelvic fascia on left side of prostate and drain prevesical space.

legs are put flat, somewhat spread apart, the whole procedure having taken but 2 or 3 minutes. Now the retropubic prostatectomy is proceeded with. After the prostate has been removed and the capsule sutured, the right forefinger is again introduced into the previously made tract in the perineum where its tip can be felt by the other hand in the abdomen just to the left of the prostate and covered by the endopelvic fascia. Although this fascia is not very thick, it is rather tough and difficult for the finger to break through. Consequently, a long, sharpish instrument, such as a dura clip applicator, is employed from above to make an opening in this fascia from the inside of the pelvis down on the finger, which is then pushed up through, thus establishing the drainage tract (fig. 3, *C*). Through this tract a soft rubber wick (Penrose) is placed to drain the prevesical space down through the perineum, where it is secured to the skin with a silk suture (fig. 3, *D*). The abdominal wound is closed without drainage. The urethral cathe-

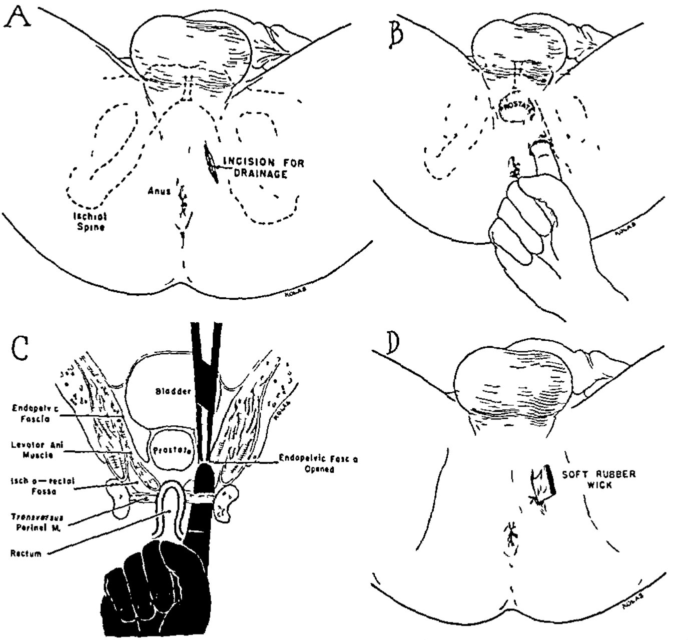

FIG 3 *A*, technique of operation With thighs somewhat flexed and separated, an 1 inch incision is made above and to left of anus. *B*, forefinger passes under transversus perine muscle, and then up left side of ischiorectal fossa to left lobe of prostate *C*, coronal section showing long pointed instrument (dura clip applicator) making opening from above in endopelvic fascia on tip of finger establishing drainage tract *D*, perineal drain in place sutured to skin It will not be "started" until 2 days after urethral catheter has been removed Abdominal wound closed without drainage

ter is left in place for one week, and the perineal drain is not "started" until 48 hours after the urethral catheter has been removed.

This technique has now been used in 8 cases in recent months with satisfactory results The suprapubic wounds have healed cleanly and without draining There has been no osteitis pubis, no unexplained bouts of fever, and no interference with urinary control The only complication occurred in the second case; the senior author, when the time came to put the right forefinger back into the previously made tract and break through into the prevesical area, while feeling under the drapes inadvertently put his finger into the anus He accomplished the break through into the prevesical space but with more difficulty than usual The reason for this became apparent when he placed the drain, and he was horrified to find that he had drained the prevesical space into the rectum by means of a good-sized hole For a moment ideas of such things as a proximal diverting colostomy were entertained, but then it was decided to see what

Mother Nature would do, and nothing was done other than to replace the drain in the proper perineal tract to the prevesical space and close the abdominal wound as usual, no attempt being made to repair the hole in the rectum which was hard to visualize. The urethral catheter was left in place longer than usual (2 weeks) and the drain removed 3 days later. Fortunately, no fistula of any sort occurred. However, 3 days after the removal of the drain, a small abscess pointed subcutaneously at the drain site. This was easily opened on the ward with Kelly forceps, and an ounce or so of frank pus evacuated, following which solid healing took place. The patient left the hospital in good condition and with normal voiding. He has been seen several times in the followup clinic and has continued to do nicely. Since that case the finger has always been reintroduced into the perineal drainage tract under vision. Although this mistake sounds inexcusable, it is not hard to make when working blindly under drapes, as the drainage tract and the anus are not far apart.

SUMMARY

The retropubic prostatectomy is an excellent operation for the treatment of benign prostatic hypertrophy, but osteitis pubis has followed this procedure in a small but significant percentage of cases and is a potential drawback to this operation.

There is evidence to show that infection in the prevesical space is the important factor in the etiology of osteitis pubis.

The prevesical space (space of Retzius or retropubic space) usually becomes contaminated and thus is exposed to possible infection during retropubic prostatectomy, and its poor natural drainage favors the development of infection unless it is drained properly.

The authors feel that dependent drainage of the prevesical space via the perineum must be more efficient than the usual suprapubic "uphill" drainage, and therefore should be better prophylaxis against the development of infection there, and thus against the occurrence of osteitis pubis. This procedure has been carried out in 8 cases in recent months with satisfactory results. The technique is described.

Addendum: (October 22, 1955): Since our paper was written, the procedure has been continued so that now it has been carried out in a total of 20 cases. The results have continued to be satisfactory in all cases.

The Journal of Urology
Vol 75 No 3 March 1956
Printed in U S A

UROLOGICAL COMPLICATIONS OF SPINA BIFIDA IN CHILDREN

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The future of the child born with spina bifida has improved considerably In 1918, Frazier[1] wrote that eighty to ninety per cent of such children died during their first year and of the small percentage remaining, the majority were mentally defective and physically crippled The operative mortality was forty to sixty per cent [2-5] Except in the simplest forms of spina bifida, the tendency had been to defer operation, thus dooming these children to almost certain death However, with improvements in neurosurgical methods and the advent of antibiotics, the majority of these children are now able to survive the critical first year of life [6, 7] Rapid strides in the field of orthopedic surgery have made possible the correction of practically all associated deformities in the growing child As a result of recent advances in rehabilitative therapy, the spina bifida paraplegic child can now be taught to care for his daily needs within the limits of his disability, ambulate with braces and crutches, and have the opportunity to take his place eventually as a self-dependent and productive member of society [8]

Total rehabilitation in this group of patients has, however, been seriously impeded by two factors, namely, 1) urinary incontinence and 2) progressive renal damage Unsatisfactory control of urination has made these children malodorous, uncomfortable and socially unacceptable The development of destructive lesions in the kidneys undoubtedly is the major cause of decreased life expectancy The number of spina bifida children with paraplegia who survive early adulthood, although not accurately known, is probably small

The solution to these problems obviously devolves on the urological member of the team of specialists concerned with the care of these children A survey of the nature and frequency of the changes occurring in the urinary system of the spina bifida child is therefore warranted, a better understanding of the pathophysiology of such changes may lead to improved methods of therapy

Accepted for publication October 24, 1955

This investigation was supported by a research grant (B 374 C) of the National Institutes of Health, United States Public Health Service

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TABLE 1. *Age and sex (34 cases)*

Ages of Patients	
0–5	12
6–10	12
11–15	7
16–20	3
Sex of Patients	
Males	16
Females	18

TABLE 2. *Site and variety of spina bifida (34 cases)*

Site	
Cervical	1
Thoracolumbar	2
Lumbar	3
Lumbosacral	26
Sacral	2
Variety	
Meningomyelocele	21
Meningocele	11
Spina bifida occulta	2

TABLE 3. *Associated congenital anomalies*

Arrested hydrocephalus	15
Club feet	20
Dislocation of hips	7
Erb's palsy	1

TABLE 4. *Motor disturbances (34 cases)*

Paraplegia	
Complete	23
Incomplete	9
Quadriplegia	
Complete	0
Incomplete	1
No motor disturbances	1

was located in the cervical region in one case, thoracolumbar in two, lumbar in three, lumbosacral in twenty-six, and sacral in two. There were twenty-one instances of meningomyeloceles, eleven meningoceles, and two spina bifida occulta.

The following associated congenital anomalies (table 3) were encountered: arrested hydrocephalus, 15 patients; club feet, twenty; dislocation of the hips, seven; and Erb's palsy, one.

Table 4 lists the motor disturbances involving the patients in this series. Com-

TABLE 5. *Urinary symptoms (34 cases)*

Recognition of desire to void	
Complete absence	26
Vague sensations	8
Ability to initiate micturition	
Absent	2
Present	32
Initiation of micturition	
All cases were incontinent	

plete paralysis of the lower extremities was present in 23 children and partial paralysis in nine. One patient with cervical meningocele had spastic quadriparesis. No motor deficiency was noted in one patient whose only manifestation of the disease aside from radiographic findings was inability to control urination.

It is noteworthy that largely as a result of the habilitation program to which the children in this series have been subjected, nineteen of them are now able to ambulate with braces and/or crutches. The remaining fourteen, excluding the 1 case without motor disability, are now capable of wheel chair activities and should be able to achieve ambulation eventually when they are older and develop more strength in their arms.

ANALYSIS OF CASES

Symptoms. Inquiries were made into the three essential components of voiding, namely, the desire to void, initiation of micturition, and its inhibition. The information was obtained from the child, parent, or nurse.

Urinary control was unsatisfactory in all the cases (table 5). Twenty-six children could not recognize the desire for urination. The other eight claimed to have a more or less vague sensation of fulness, the significance of which they were not cognizant. No aurae of impending micturition such as flushing of the face, headaches, goose pimples or sweating were experienced by any of the patients.

Practically all the patients could initiate micturition when requested to do so by straining and applying Credé pressure. Urine escaped in a stream which was continued only so long as the pressure was constantly maintained. One case of cervical spina bifida voided spontaneously, while another with severe scoliosis and lordosis could not expel her urine voluntarily despite straining and manual compression.

Prior to the institution of a voiding schedule, the majority of the children made no conscious efforts to urinate. Micturition occurred by overflow and emptying was obviously incomplete.

In spite of adherence to a voiding schedule, inhibition of micturition could not be accomplished. Constant dribbling or intermittent spurts of urinary leakage occurred shortly after each voluntary urination and were exacerbated by movements or straining efforts.

Varying degrees of rectal incontinence were present in practically all the cases, although this could usually be handled fairly well by establishing a scheduled time for bowel evacuation and with the aid of glycerine suppositories.

Cystourethrography. Cystograms were done to determine the degree of trabecu-

TABLE 6. *Cystographic findings (34 cases)*

Smooth bladder wall	9
Trabeculations	
Moderate	13
Marked with cellules	12
Vesicoureteral reflux	9

lation and cellule formation, and to reveal the presence of diverticulum and vesicoureteral reflux. Urethrograms may show the condition of the vesical neck but are of limited usefulness.

The bladder was filled with approximately 75 cc of contrast medium, injected through a urethral catheter. The catheter was then removed and an anteroposterior x-ray film taken. Urethrograms were also secured in male patients by injection of dye into the urethra with an asepto syringe. A second film was taken in the right oblique position, and a third or delayed film 20 minutes later.

The cystographic findings are given in table 6. The bladder was smooth in 9 cases, moderately trabeculated in thirteen, and markedly trabeculated with cellule formation in twelve. No large-sized bladder diverticulum was demonstrated in any of the patients. Vesicoureteral reflux was present in 9 children, unilaterally in seven and bilaterally in two. The reflux was associated with massive hydronephrosis in 5 cases, moderate in three, and normal pelvis and calyces in one. One patient had reflux demonstrable only in the delayed film, but this was subsequently reproducible 6 months later in all the films together with pyelectasis and caliectasis.

Cystoscopy. A cystoscopic examination is of value in assessing the severity of bladder infection, revealing the presence of bladder calculi and diverticula, and determining the amount and degree of trabeculation. The presence of spasticity or contraction of the vesical neck is hard to determine by cystoscopy.

Cystoscopy was performed in 19 patients (table 7). The bladder mucosa exhibited a mild degree of congestion in all cases, indicating slight urinary infection. No intense inflammatory process was observed in any of the bladders examined. Unlike adult paraplegics, not a single patient had bladder calculi, nor was any large diverticulum visualized. The amount and degree of trabeculations observed during cystoscopy conformed to the cystographic findings.

Excretory urography. Excretory urograms reveal both the anatomy and function of the kidneys. In order to evaluate the renal changes, the following classification was used:

Normal: Normal excretory urogram
Grade 1: Minimal hydronephrosis
Grade 2: Definite hydronephrosis
Grade 3: Massive hydronephrosis
Grade 4: Nonfunctioning kidney by intravenous pyelogram

TABLE 7. *Cystoscopic findings (19 cases)*

Moderate congestion	19
Calculus formation	0
Diverticulum (large)	0

TABLE 8. *Classification of pyelographic findings*

	No of Kidneys	Percentage
Normal	51	75.0
Grade 1	4	5.9
Grade 2	4	5.9
Grade 3	8	11.8
Grade 4	1	1.4

TABLE 9. *Relation of pyelographic findings to variety of spina bifida*

	No of Kidneys	Normal	Grade 1	Grade 2	Grade 3	Grade 4
Occulta	4	4 (100%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Meningocele ...	22	17 (77%)	2 (9%)	2 (9%)	0 (0%)	1 (5%)
Meningomyelocele	42	30 (71%)	2 (5%)	2 (5%)	8 (19%)	0 (0%)

In table 8, the excretory urograms obtained on the 34 patients are classified according to the preceding criteria. The pyelograms are tabulated in terms of individual kidneys. It will be noted that 51 kidneys (75 per cent) were graded as normal, and the remaining 17 kidneys (25 per cent) showed pathological changes. Of these, 4 kidneys (5.9 per cent) were considered as grade 1, four kidneys (5.9 per cent) were grade 2, eight kidneys (11.8 per cent) were grade 3, and 1 kidney (1.4 per cent) was grade 4.

The relation between the incidence of renal damage to the variety of neural lesion is shown in table 9. Renal damage occurred in approximately the same percentage in meningoceles and meningomyeloceles. Although there was only a limited number of cases of spina bifida occulta in our series, it is reasonably certain that associated destructive lesions in the kidney would be infrequent.

The incidence of pathological kidney changes in relation to age is tabulated in table 10. Renal damage was greatest in incidence and severity between the ages of 6 and 10 years, after which a decline occurred in the succeeding age groups. It is improbable that an improvement in renal status was responsible for the decrease in the frequency and intensity of destructive lesions in the older age groups because the majority did not have any planned urologic care prior to their inclusion in this series. Rather, it suggests that most of the deaths arising from kidney damage occur between the ages of 6 and 10 years, which should therefore be regarded now as the critical period in the life of a child with spina bifida.

Cystometry. A cystometrogram is a graphic record of vesical activity. The fol-

TABLE 10. *Relation of pyelographic findings to age of patient*

Age Group	No of Kidneys	Normal	Grade 1	Grade 1	Grade 2	Grade 3
0–5	24	21 (88%)	0 (0%)	1 (4%)	2 (8%)	0 (0%)
6–10	24	14 (58%)	2 (8%)	3 (13%)	4 (17%)	1 (4%)
10–15	14	11 (79%)	2 (14%)	0 (0%)	1 (7%)	0 (0%)
16–20	6	5 (83%)	0 (0%)	0 (0%)	1 (17%)	0 (0%)

lowing data may be obtained during the procedure 1) intracystic pressure in relation to bladder volume, 2) presence or absence of reflex contractions of the bladder muscle and measurement of their amplitude, 3) maximum voluntary intravesical pressure during abdominal straining, 4) presence or absence of vesical sensations, 5) bladder capacity

In this investigation, a Lewis aneroid cystometer and a simple water manometer were connected by a Y-tube to an indwelling catheter This arrangement furnished a continuous recording of pressure changes and allowed detection of small contraction waves or slight changes in intravesical pressure

Fluid was introduced into the bladder from a reservoir equipped with a Murphy drip and calibrated so that the number of cubic centimeters of fluid introduced would be easily read The rate of flow was controlled by a Hoffman screw clamp

Pressure changes were observed 1) after each addition of 25 cc fluid increments, 2) during introduction of fluid at a slow constant rate (11 drops/min), and 3) while allowing the bladder to fill by excreted urine

Figure 1, *A* depicts vesical activity in an 8 year old spina bifida paraplegic boy during introduction of 25 cc increments of fluid at 1 minute time intervals through a suprapubic cystostomy tube It will be noted that with each additional quantity of fluid, there was a steep rise in intravesical pressure which slowly diminished to a resting level An initial rise in the resting pressure occurred, which, however, was sustained at about 30 mm Hg after the third injection of fluid, at which time urine started to escape from the urethra with each further addition of fluid This pressure curve demonstrates the tendency of the spina bifida bladder to resist suddenly injected fluid, indicating poor adaptation to stretch

Figure 1, *B* shows the cystometric graph from the same patient when fluid was introduced at a slow steady drip (100 drops/min) The pressure curve was flat and contained no forceful sustained contraction Superimposed were small rhythmical waves indicating minor ineffectual contractions Although the patient dribbled urine continually during the determination, bladder tonus was sustained at 10–15 mm Hg A similar type of recording was obtained when the bladder was allowed to fill by excreted urine (fig 1, *C*)

During the early part of this investigation, several of our recordings obtained from a water manometer erroneously showed "hypertonic" pressure curves It can now be readily seen that such a record can be expected to occur when inadequate time is allowed between adding increments of fluid or when fluid is steadily but rapidly run into the bladder

Residual urine determination Residual urine is the result of the inability of the bladder to empty completely, because of inefficient detrusor action or increased resistance at the vesical neck, or a combination of both It has been generally accepted that this is the primary disturbance responsible for most of the problems associated with neurogenic vesical dysfunction among adult paraplegics, and its elimination will minimize such problems The presence of more than 100 cc residual urine has been regarded arbitrarily as an indication for definitive treatment

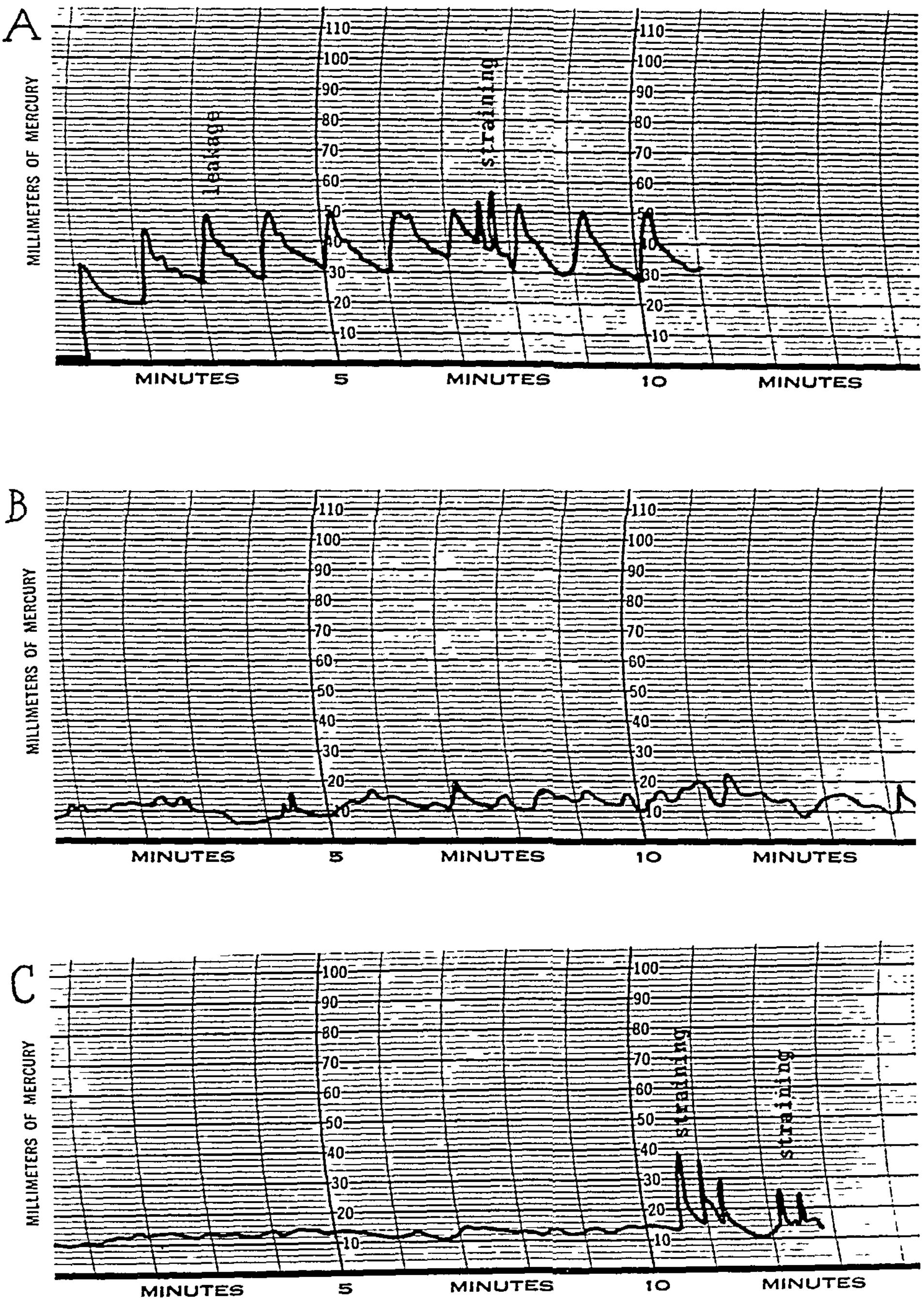

FIG. 1. Cystometrograms in 8-year-old spina bifida paraplegic boy during *A*, addition of 25 cc fluid increments at one minute intervals; *B*, introduction of fluid at a slow constant rate (100 drops/min.); and C, bladder filling by excreted urine.

Residual urine was measured after voiding with the aid of intrinsic (strain) and extrinsic (Credé) pressures. Only 5 cases had more than 60 cc residual urine, 24 cases had less than 60 cc, and five had no residuum (table 11).

Of the 5 cases with large volumes of residual urine, three had moderate hydro-

TABLE II *Residual urine determination (34 cases)*

More than 60 cc	4
Less than 60 cc	25
No residuum	5

nephrosis without demonstrable reflux, and the other two had normal pelvis and calyces Nine cases of hydronephrosis, including the most advanced lesions in this series, were encountered among patients who had little residual urine or none whatsoever Reflux was demonstrable in all belonging to the latter group

TREATMENT

There are two phases in the management of the child with neurogenic vesical dysfunction due to spina bifida, namely, 1) correction of urinary incontinence, and 2) treatment of progressive renal damage

Correction of urinary incontinence The long list of procedures advocated for correction of neurogenic bladder incontinence suggests that no one of them has been completely adequate

a Bladder training As part of their training in self care, the children in this series were placed routinely on a bladder training program,[8, 10] except when vesicoureteral reflux was demonstrated by cystography They learned to use the toilet or commode rather than a bedpan, utilized different methods of initiating micturition, followed a voiding schedule regulated fluid intake, observed genital cleanliness, changed their pads and rubber pants, and later became familiar with the use and care of a urinal bag and other rubber appliances

Contrary to previous clinical impressions,[8] no child in this group was able to achieve urinary continence Bladder training has, however, brought about increased independence in the child's daily needs and lessened the amount of wetting Urinary diversion either with an inlying catheter or suprapubic cystostomy is indicated when incontinence remains intolerable despite all efforts Rubber urinals have slightly improved the situation among the older boys, but no satisfactory appliance has been devised for girls

b Laminectomy Exploration of the spinal cord was favored by Chute[11] and Mertz,[12] who reported successful results following relief of traction or pressure from cord structures Despite reports of improvement or cure in an occasional case, the successes following this procedure are few Alexander and his associates[13] reported one case where bladder continence was gained apparently as a result of the crushing of the S 3 nerve roots

c Sphincter operations Numerous operations have been performed in which

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[10] Munro, D The rehabilitation of patients totally paralyzed below the waist, with especial reference to making them ambulatory and capable of earning their living III Tidal drainage, cystometry and bladder training New Eng J Med , 236 223-235, 1947

[11] Chute, A L The relation between spina bifida occulta and certain cases of retention J Urol , 5· 317-324, 1921

[12] Mertz H O and Smith, L A Posterior spinal fusion defects and nerve dysfunction of the urinary tract J Urol , 24: 41-82, 1932

[13] Alexander, E , Garvey, F K and Boyce, W Congenital lumbosacral myelomeningocele with incontinence A contribution to the understanding of bladder physiology J Neurosurg , 11. 183-191, 1954

muscle or fascial strips were placed in a sling or pseudosphincter fashion about the bladder neck or posterior urethra. Varying degrees of success have been reported, but in general, they have not been encouraging. Smith and Engel[14] used the gracilis muscle, Miller[15] employed the pyramidalis muscle, and Ewert and Flint[16] passed a flap of rectus muscle and fascia around the posterior urethra to form an artificial sphincter. We utilized the last procedure in 2 cases with no success.

d. Transurethral resection: Workers from the Mayo Clinic have reported relief of incontinence following transurethral resection of the vesical neck.[17, 18] This form of therapy would be applicable only for the minority whose urinary incontinence is associated with retention.

e. Urinary diversion: The use of an indwelling Foley catheter connected to a rubber urinal appliance affords the simplest way of diverting the urinary stream. This arrangement, however, is at best only a temporary measure. The frequent irrigations and changes of the catheter which must be carried out are inconvenient to the child and his parents. Protracted use of the urethral catheter is complicated by urethral sepsis and vesical calculus formation.

In our experience, a suprapubic cystostomy has represented the best method for urinary diversion. Of 5 children in this series who have cystostomy drainage, four are able to remain dry and comfortable. We have observed that when the suprapubic tube is connected to open drainage, the bladder can usually be kept sufficiently empty so that the small remaining sphincteric tonicity is sufficient to retain the small amount of urine constantly present in the cystostomized bladder. Leakage will, of course, occur when the tube is clamped, but this occasion will rarely arise when a rubber collecting appliance is available. We do not believe that surgical closure of the urethra should be done at the time of cystostomy as advised by others,[19] although it may have to be resorted to later in the cases where simple cystostomy fails.

Once cystostomy is properly established, the child's parents rarely encounter difficulty in caring for the tube. Daily saline irrigations can easily be done by the child or parents and the catheter is usually changed once a month.

Other workers have advocated more radical procedures to relieve incontinence. The so-called "wet colostomy" which consists of a ureterosigmoid anastomosis and an end sigmoidostomy has been tried and found unsatisfactory because of the foul odor from intermixture of urine and feces, and the high incidence of ascending urinary infection.[19] Artificial bladders using the cecum[20] or sigmoid[19] to

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[14] Smith, C. K. and Engel, L. P.: Neurogenic vesical dysfunction in children. J. Urol., **28**: 675–715, 1932.

[15] Miller, N. F.: The surgical treatment of urinary incontinence in the female. J.A.M.A., **98**: 628–632, 1932.

[16] Ewert, E. E. and Flint, F. D.: Rectus muscle sling for neurogenic incontinence. Surgery, **27**: 688–698, 1950.

[17] Thompson, G. J. and Jacobson, C. E.: Neurogenic vesical dysfunction due to spina bifida and myelodysplasia. Treatment by transurethral resection of the vesical neck Am. J. Surg., **61**: 223–238, 1943.

[18] Emmett, J. L. and Helmholz, H. F.: Transurethral resection of the vesical neck in infants and children. J. Urol., **61**: 463–478, 1948.

[19] Gross, R. E., Holcomb, G. W. and Swan, H.: Treatment of neurogenic urinary and fecal incontinence in children. Arch. Surg., **66**: 143–154, 1953.

[20] Gilchrist, R. K., Merricks, J. W., Hamlin, H. H. and Rieger, I. T.: Construction of a substitute bladder and urethra. Surg., Gynec. & Obst., **90**: 752–760, 1950.

act as reservoirs with a small opening on the anterior abdomen have been constructed. The following complications have been encountered after such bladder substitutions: 1) leakage or retention of urine from too large or too small an opening, 2) spasms of the isolated segment of bowel causing abdominal pain, 3) calculus formation, 4) ulceration and bleeding, and 5) rupture of the pouch. The Bricker procedure[21] which utilizes an isolated piece of the terminal ileum to convey the urine from both ureters to an external stoma has been tried by Bill and his co-workers[22] on a case of spina bifida with encouraging results. The end-results following such extensive operations, however, do not justify the risks involved, especially when one considers that just as much can be accomplished with a simple suprapubic cystostomy.

Treatment of progressive renal damage. The progressive deterioration of the upper urinary tracts has been a very vexing problem and represents the most serious complication of spina bifida in children. In the past, various surgical procedures such as nephrostomy, pyelostomy, cutaneous ureterostomy and cystostomy have been tried, yielding inconclusive clinical benefits.

Our present policy is to institute continuous drainage either with an inlying catheter or suprapubic cystostomy whenever there is evidence of renal damage. These procedures afford the least interference to the spina bifida child's activities of daily living. In the presence of a large residual urine, a transurethral resection of the vesical neck may be performed and bladder decompression deferred, provided the kidney lesion is not severe.

Ureteral plastic procedures may be employed in cases of advanced hydronephrosis with extensive ureteral dilation and angularity. The tortuous ureters are freed throughout their entirety from the bladder to the kidney pelvis and the straightened proximal segments are reimplanted into the bladder after resection of the redundant distal portions. This procedure is designed to reduce urinary stasis and promote dependent renal drainage. Improvements in the upper urinary tract status were observed in 4 patients treated in this manner.

We are not certain, however, whether simple cystostomy drainage alone might suffice to relieve the ureteral dilation and tortuosity and result in reduction of the hydronephrosis present in advanced cases. Our studies are still incomplete and further observations will be necessary before definitive rules can be set.

In extreme cases characterized by continued septic temperature elevations despite bladder drainage, nephrostomy may be necessary and life saving. We had to resort to this procedure, however, in only 1 case.

Followup care. These patients must be followed with the utmost vigilance as long as they live. Excretory urography, cystography, and estimation of residual urine should be made every 6 months even in the absence of symptoms. It should be borne in mind that dangerous renal lesions may develop insidiously and a bladder that empties well is no guarantee for the permanency of good renal function.

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[21] Bricker, E. M. Bladder substitution after pelvic evisceration. S. Clin. N. Amer., 30: 1511–1521, 1950.

[22] Bill, A. H., Dillard, D. H., Eggers, H. E. and Jensen, O. Urinary and fecal incontinence due to congenital abnormalities in children. Management by implantation of the ureters into an isolated ileostomy. Surg. Gynec. & Obst., 98: 575–580, 1954.

DISCUSSION

The neurophysiology of the bladder disturbances occurring in spina bifida have been discussed by various authors.[13, 14, 23, 24] Most workers now agree that they are comparable to those observed in patients who have been rendered paraplegic or paraparetic by trauma, tumor or infection. The nature of the neurogenic vesical dysfunction will depend on the level and extent of involvement of the spinal cord and its nerve roots.

Inasmuch as the majority of spina bifida are situated in the lumbosacral vertebrae, the resulting vesical changes bear many points of resemblance to those seen with the acquired lesions of the sacral portion of the spinal cord and the cauda equina. This type of disturbance is referred to as the autonomous type of neurogenic vesical dysfunction. The parasympathetic innervation of the bladder which comes from the sacral segment of the spinal cord has been partially or completely destroyed. The bladder, except for its sympathetic innervation, is completely divorced from the central nervous system. Any activity in the detrusor muscle and internal sphincter must apparently occur as the result of impulses transmitted through a reflex arc that lies wholly within the vesical wall. Such a bladder, because of its self-governing or autonomous character, is called an autonomous bladder.

The following features may be observed: 1) A powerful sustained contraction of the detrusor muscle characteristic of reflex micturition is not possible, 2) abdominal straining has replaced detrusor contraction as the expulsive force in voiding, 3) spontaneous contraction waves of small amplitude occur during bladder filling, 4) the detrusor muscle resists rapid filling of the bladder.

It is obvious that the incontinence in spina bifida is the consequence of flaccid urinary sphincters. A more or less constant urinary leakage increased by bodily movements is the usual finding. Although this type of incontinence has been described or recognized by others in connection with cauda equina or low spinal cord injuries,[25, 26] it is well known that its occurrence in traumatic lesions of the spinal cord is relatively infrequent. Neither does it occur, except in few cases, following subarachnoid alcohol block,[27] sacral rhizotomy,[28] or cordectomy,[29] all of which cause paralysis of the urinary sphincters. Watkins believes that urine does not escape from the bladder in lesions of the conus and cauda equina despite paralysis of the external sphincter and incompetence of the internal sphincter

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[23] Mertz, H. O.: The relation of spina bifida occulta to neuromuscular dysfunction of the urinary tract. J. Urol., **29:** 521–530, 1933.

[24] Langworthy, O. R., Kolb, L. C. and Lewis, L.: Physiology of Micturition. Baltimore: Williams & Wilkins Co., 1940, pp. 80–87.

[25] Munro, D.: Rehabilitation of veterans paralyzed as the result of injury to the spinal cord and cauda equina. Am. J. Surg., **75:** 3–18, 1948.

[26] Denny-Brown, D. and Robertson, E. G.: The state of the bladder and its sphincters in complete transverse lesions of the spinal cord and cauda equina. Brain, **56:** 397–462, 1933.

[27] Bors, E.: Bladder disturbances and the management of patients with injury to the spinal cord. J. Internat. Coll. Surg., **21:** 513–527, 1954.

[28] Brendler, H., Krueger, E. G., Lerman, P., Harper, J. G., Bradley, D., Berman, M. H., Hertzberg, F., Lerman, F. and Dean, A. L.: Spinal root section in treatment of advanced paraplegic bladder. J. Urol., **70:** 223–229, 1953.

[29] McCarthy, C. S.: The treatment of spastic paraplegia by selective spinal cordectomy. J. Neurosurg., **11:** 539–545, 1954.

because of the existence of considerable mechanical resistance to the outflow of urine, brought about by the pressure and elasticity of the tissues surrounding the urethra in the region of the triangular ligament.[30] Such a resistance to the urine outflow is not expected in spina bifida lesions in view of the flaccid paralysis and atrophy of the perineal muscles.

Certain bladder complications like calculosis, urinary stasis and severe cystitis are, however, infrequent in spina bifida. Not a single calculus was observed in this series, in contrast to the 15 to 70 per cent incidence among adults with traumatic paraplegia.[29, 31, 32, 33] Although other workers have reported a higher percentage of spina bifida patients who carry substantial amounts of residual urine,[17, 18, 34] the majority of our cases had little residual urine or none whatsoever. Cystitis characterized by an intense inflammatory reaction of the bladder and foul turbid urine were not encountered in any of the patients.

Unlike his adult counterpart, the child who has spina bifida does not go through any prolonged period of recumbency and immobilization which is a major precipitating factor in calculus formation. Bladder emptying is facilitated by the relaxed sphincters. In the absence of calculi and urinary stasis, urinary infection is expectedly minimal.

It has been commonly believed in the treatment of paraplegics that the health of the upper urinary tract is dependent upon the health of the bladder. Hydronephrosis is usually traceable to stasis and infection in the bladder. The frequency of occurrence of advanced hydronephrosis and ureterectasis among patients in this study who carried moderate amounts of residual urine or none whatsoever, and with mild urinary infection, indicates that one cannot prognosticate the future of the kidneys by judging bladder function.

It is more probable that vesicoureteral reflux was largely responsible for the renal complications in the majority of our patients. The etiology of reflux is still poorly understood, but it is apparent from our study that stasis of urine in the bladder, if at all, plays only a minor role.

After an extensive study, Graves and Davidoff[35] came to the conclusion that a well sustained tonus of the bladder musculature as it resists filling plays an important role in the causation of reflux. Our cystometric data and the findings of advanced trabeculation substantiate this hypothesis.

SUMMARY

As a result of advances in the fields of neurosurgery, orthopedics, and rehabilitative therapy, the spina bifida paraplegic child now has an opportunity to take his place eventually as a self-dependent and productive member of society. Total rehabilitation has, however, been seriously impeded by two factors, namely, 1) urinary incontinence and 2) progressive renal damage.

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[30] Watkins, K. H. The bladder function in spinal injury. Brit. J. Surg., **23:** 734–759, 1936.

[31] Bumpus, H. C., Nourse, M. H. and Thompson, G. J. Urologic complications in injury of the spinal cord. J.A.M.A., **133:** 366–369, 1947.

[32] Petroff, B. The paralyzed patient. Urologic aspects. J.A.M.A., **129:** 154–155, 1945.

[33] Bors, E. Urological aspects of rehabilitation in spinal cord injuries. J.A.M.A., **146:** 225–229, 1951.

[34] McCarroll, H. R. Spina bifida urinary incontinence. A report of cystometric studies in a series of 30 cases with some suggestions regarding their clinical management. Surg. Gynec. & Obst., **64:** 721–737, 1937.

[35] Graves, R. C. and Davidoff, L. M. Studies on the ureter and bladder with especial reference to regurgitation of the vesical contents. J. Urol., **10:** 185–231, 1923.

Data obtained in a survey of the nature and frequency of the changes occurring in the urinary system of a group of thirty-four spina bifida children are presented. Our experience in their urological treatment and care is also discussed.

Unsatisfactory control of urination characterized by a more or less constant urinary leakage increased by bodily movements was the usual finding. Cystoscopy revealed the presence of trabeculations in the majority of bladders examined. Cystography demonstrated reflux in 9 children (26 per cent), unilateral in seven and bilateral in two. Cystometric study showed that the spina bifida bladder has the characteristic features of an autonomous type of neurogenic vesical dysfunction.

Evidence of renal destructive lesions was noted in seventeen (25 per cent) of 68 kidneys studied during excretory urography. Renal damage was greatest in incidence and severity between the ages of 6 and 10 years, after which a decline occurred in the succeeding age groups. It is probable that most of the deaths from kidney complications occur between the ages of 6 and 10 years, which should therefore be regarded now as the critical period in the life of the spina bifida child.

Bladder training was instituted routinely as part of the self-care program, except when reflux was demonstrable. Although continence was not achieved in any of the cases, it has brought about increased independence in the child's daily needs and lessened the amount of wetting. Urinary diversion either with an inlying catheter or suprapubic cystostomy is advisable when incontinence remains intolerable despite all efforts.

Continuous bladder drainage, either with an indwelling urethral catheter or suprapubic cystostomy, should be established whenever there is evidence of renal damage. If the residual urine is large, transurethral resection of the vesical neck may be performed and bladder decompression deferred, provided the kidney lesion is not severe.

Four patients with advanced hydronephrosis and extensive ureteral dilation and angularity were treated by freeing the ureter, reimplanting the straightened proximal segment into the bladder, and resecting the redundant distal portion, thus promoting free dependent drainage of the kidney. Improvement in the upper urinary tract status followed. Studies are, however, being conducted with other patients to determine whether simple cystostomy alone will suffice in such cases.

Nephrostomy may be necessary and life-saving in extreme cases of urinary sepsis not responding to bladder drainage.

Followup examinations consisting of excretory urograms, cystograms, and residual urine determinations should be done every 6 months even in the absence of symptoms. Dangerous renal lesions may develop insidiously and a well-emptying bladder is no guarantee for the permanency of good renal function.

The authors are indebted to Mrs. Jean McCarthy Lichtenstein (nurse supervisor, Children's Division, Institute of Physical Medicine and Rehabilitation) and Mr. James Ramseur (research technician) for their assistance in this work.

The Journal of Urology
Vol. 75, No. 3, March 1956
Printed in U.S.A.

PAPANICOLAOU EXAMINATION OF URINE IN DIAGNOSIS OF URINARY CANCER: 2. FALSE POSITIVES IN DIAGNOSIS OF RENAL NEOPLASMS

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One of the most difficult problems in urologic diagnosis is the detection of early neoplasms of the kidney. There is little difficulty in identifying obvious space-consuming lesions; when the diagnosis is not evident upon exposing the kidney at operation, biopsy can be safely performed if certain precautions are taken.[1] Difficulty arises in patients with obscure hematuria that may or may not be localized to one kidney when pyelograms are normal or reveal equivocal filling defects.

In view of the inadequacy of usual methods of diagnosis, it was our hope that the Papanicolaou technique, which has served so well in other fields, might be developed as a diagnostic aid in this type of case. However, the pitfalls of the method have proved so disconcerting that they warrant serious consideration. We have collected 4 cases in which false positive Papanicolaou smears, interpreted by pathologists experienced in the technique, contributed in part to the performance of nephrectomy for what proved to be benign lesions. A positive result is considered false when cytologic study shows what are thought to be neoplastic cells, but pathologic examination of tissue removed fails to confirm the presence of neoplasm.

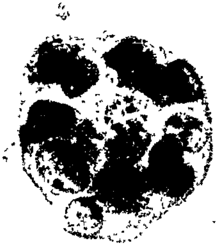

Fig. 1. Case 1. False positive smear of urine from left kidney. Cluster of cells contains enormous nuclei of different sizes and shapes.

In the 4 cases abstracted in table 1, hematuria was the presenting symptom. In two, bleeding was localized to one side of the upper urinary tract. In all in-

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Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23-25, 1955.

Supported by a State of California Department of Public Health Grant.

[1] Weyrauch, H. M., Wanless, H. L., Goebel, J. L. and Scott, K. G.: Biopsy of kidney for suspected neoplasm. J. Urol., **67**: 60-85, 1952.

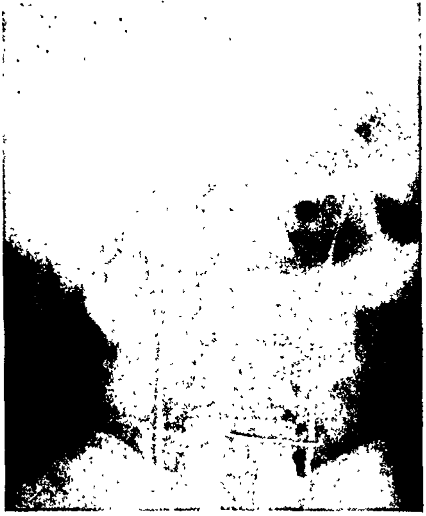

FIG. 2. Case 2. Retrograde pyelogram demonstrating elongated cephalic calyx with irregularity of infundibulum. False positive Papanicolaou smear. Findings produced by hemorrhage and edema.

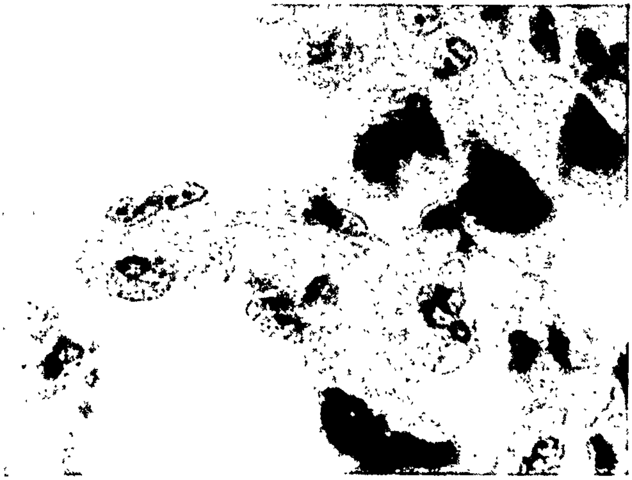

FIG. 3. Case 3. False positive smear from urine of right kidney demonstrating hyperchromasia, multinucleation and variability in shape of nuclei.

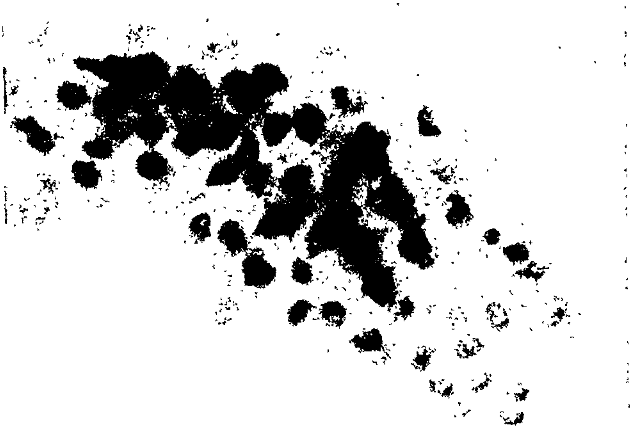

FIG. 4. Case 4. False positive smear of urine from right kidney showing cluster of well-differentiated cells with hyperchromasia and multinucleation.

TABLE 1 *Cases demonstrating false positive Papanicolaou smears of kidney urine*

Case No	Sex	Age	Complaint	Urine	Cystoscopic Findings	Pyeloureterograms	Papanicolaou Studies	Operation	Pathologic Examination
1	M	27	Painless hematuria for 2 days	RBC 0 WBC 0 Bact 0	Normal	Small, irregular filling defect minor cephalic calyx, left	Left kidney Diagnostic of malignancy (fig 1)	Left nephroureterectomy	Subacute papillitis, hyperplasia mucous membrane, cephalic calyx
2	M	43	Painless hematuria, left lumbar pain for 10 days	RBC++++ WBC occ Bact 0	Bloody urine from left ureteral orifice	Elongation and slight irregularity of infundibulum left cephalic calyx (fig 2)	Left kidney highly suspicious of malignancy	Left nephrectomy	Hemorrhagic papilla with edema, cephalic calyx
3	M	35	Painless hematuria and right lumbar pain for 10 days	RBC++++ WBC occ Bact ō	Bloody urine from right ureteral orifice	Small persistent filling defect upper portion right renal pelvis	Right kidney highly suspicious of malignancy (fig 3)	Right nephroureterectomy	Arteriolarsclerosis with bleeding into renal pelvis
4	M	38	Microscopic hematuria for 9 months	RBC+ WBC ō Bact 0	Normal	Small, persistent filling defect, minor cephalic calyx, right	Right kidney strongly positive for malignancy (fig 4)	Right nephrectomy	Normal kidney

stances, smears of urine obtained from the renal pelvis were reported as positive to highly suspicious for neoplasm after preparation by the usual Papanicolaou technique.[2] Pyelograms were either normal or demonstrated irregularities too minute to localize at operation. Following nephrectomy, pathologic examination of the operative specimens yielded the following findings: subacute papillitis, hemorrhagic edema of renal papilla, renal arteriolar sclerosis and normal kidney.

DISCUSSION

A review of the literature indicates that other workers have encountered a high incidence of false positive smears made from specimens of urine. In a series of 168 urologic cases, Chute and Williams[3] report 13 (12 per cent) incorrectly diagnosed as "positive" for urogenital cancer. Two patients of this false positive group were thought to have renal carcinoma; however, following operation one kidney was found to contain a benign cyst, and the other proved to be normal. McDonald[4] in 84 cases of suspected renal neoplasm obtained positive smears in 19; six (31 per cent) of these proved to be false positives.

Difficulties encountered in the application of the Papanicolaou technique to the urinary sediment in general and to the diagnosis of renal neoplasms in particular are:

1) The test is successfully applied only when neoplastic cells have been exfoliated into the urine. One is unable to obtain cells by scraping suspicious areas, as is possible in making smears from the cervix of the uterus. Despite the fact that fresh urine is examined, cells may have remained in the urinary tract for long periods, and frequently their nuclear and cellular structure cannot be adequately studied. Staining qualities are altered by the pH of the urine, the length of time cells remain in the urine after exfoliation and by the technique employed in preparing the smear (any drying before fixation exerts a deleterious effect).

Again, on some occasions, the exfoliated cells are so few that satisfactory interpretation is impossible. In a previous report concerning the use of the test in mass screening,[2] 22.2 per cent of the smears obtained from 1,575 individuals contained too few cells (less than six cells per smear) to allow intelligent interpretation. Furthermore, in recovering neoplastic cells from the upper part of the urinary tract, one is limited by the small amount of urine obtained by ureteral catheterization.

2) The nature of malignant lesions of the urinary tract limits use of the technique. The incidence of neoplasms of the renal pelvis is low. They constitute only 10 per cent of all renal neoplasms, yet these are the ones most likely to exfoliate. Most renal neoplasms are adenocarcinomas arising in the parenchyma. They do not invade the excretory tubules or renal pelvis to exfoliate cells into the urine until late in their development, usually after the occurrence of hematuria.

[2] Presti, J. C. and Weyrauch, H. M.: Papanicolaou examination of urine in diagnosis of urinary cancer. 1. As a test in mass screening. Trans. West Sect., A.U.A., **21:** 150–155, 1954; also J. Urol., **73:** 430–434, 1955.

[3] Chute, R. and Williams, D. W.: Experience with stained smears of cells exfoliated in urine in diagnosis of carcinoma of genito-urinary system. J. Urol., **59:** 604–618, 1948.

[4] McDonald, J. R.: Value of exfoliative cytology in genito-urinary and pulmonary disease. Am. J. Clin. Path., **24:** 684–689, 1954.

3) Many neoplasms such as papilloma of the renal pelvis exfoliate cells indistinguishable from normal transitional cells Furthermore, well differentiated, clear cell carcinomas of the kidney may fail to show cytological characteristics of malignancy Papanicolaou[5] has called attention to the fact that cells with cuboidal or columnar form are often seen in ureteral smears in benign papillary growths However, since they also occur in the absence of any growth their diagnostic significance is limited

4) On the other hand, some normal cells of the ureter and renal pelvis closely resemble neoplastic cells Whether actually exfoliated or separated from the normal mucosa by ureteral catheter, many of these cells vary considerably in size, form and structure, far beyond the range observed in other types of exfoliated cells [6] The nuclei may have a fine chromatin network suggestive of proliferative activity Nuclear enlargement alone, therefore, is not a valid criterion of malignancy in the ureteral specimen An additional normal characteristic of cells in urine obtained by ureteral characterization is two or more nuclei Papanicolaou[5] thought that giant, multinucleated cells are syncytia formed by a fusion of many cells, probably after exfoliation, since such cells are not seen in histologic sections of the ureter or pelvis, smaller, multinucleated cells are sometimes found in the renal tubules Other possibilities are that the cells enlarge as the result of trauma during ureteral catheterization or from amitotic or mitotic division of the nucleus without a corresponding division of the cytoplasm

5) Finally, atypical transitional cells with apparent hyperchromasia may be caused by inflammatory processes or renal calculi and lead to false positive interpretation [5] These are small or medium sized cells with deeply staining nuclei usually intermixed with inflammatory cells and erythrocytes

CONCLUSIONS

In view of these considerations, when the Papanicolaou technique is applied to the diagnosis of neoplasms of the upper urinary tract, these precautions are essential

1) Criteria of what constitutes neoplastic cells of the upper part of the urinary tract must be more stringent than criteria for cells obtained directly from tissue Conclusive positive diagnosis should be based, not on one or two criteria, but upon as many neoplastic aberrations* as possible (fig 5)

2) It is essential to make smears of the urine repeatedly Interpretation should not be based on one examination alone

3) Urine from the bladder should be examined as a control before obtaining specimens from the renal pelvis Look with doubt on suspicious cells obtained from the renal pelvis when similar cells are not present in urine previously obtained from the bladder

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[5] Papanicolaou, G N Atlas of Exfoliative Cytology Cambridge, Mass Harvard University Press, 1954

[6] Papanicolaou G N Cytology of urine sediment in neoplasms of urinary tract J Urol 57 375 1947, also J Urol 57 375 1947 and Trans Am Assoc Genito Urin Surg, 38 145–147 1947

* Criteria of malignancy Marked nuclear enlargement, hyperchromasia, anisocytosis anisokaryosis multinucleation, crowding and engulfment

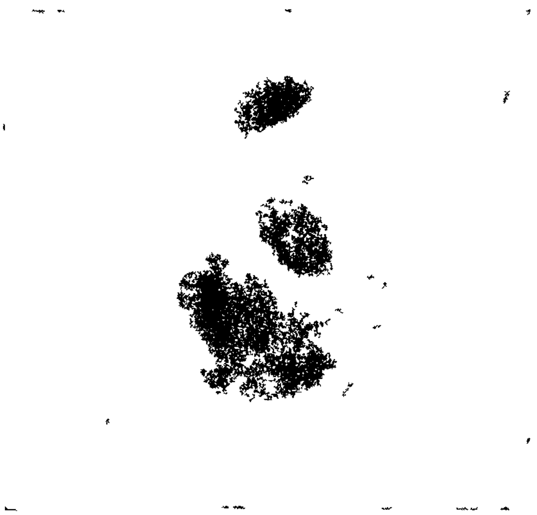

FIG 5. True positive smear from urine of left kidney demonstrating cluster of cells with multinucleation, hyperchromasia, anisocytosis and marked nuclear enlargement Left nephroureterectomy performed. Specimen showed small epidermoid carcinoma of renal papilla.

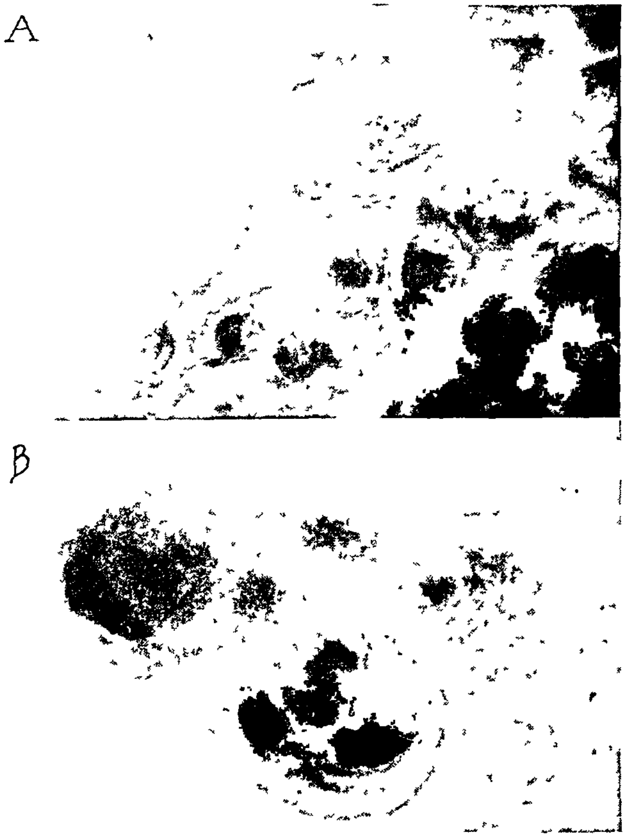

FIG. 6. Smears from right and left kidney in same patient; both are compatible with malignancy, but prolonged observation indicated they are both false positives. *A*, right kidney. Nuclei are large and hyperchromatic with prominent nuclear border. *B*, left kidney. Clump of cells demonstrates multinucleation, hyperchromasia and anisocytosis

4) Urine should always be collected from both renal pelves for comparison (fig. 6). It is important to obtain urine not only from the side on which suspicion rests, e g , when there is a pyelographic filling defect or bleeding from one kidney, but from the supposedly normal side as well.

SUMMARY

Four cases are presented in which Papanicolaou smears of urine obtained by ureteral catheterization were highly suspicious or positive for malignancy, yet careful pathological examination after nephrectomy failed to reveal evidence of neoplasm. Attention is called to the high incidence of false positive smears in the examination of renal specimens of urine, and other difficulties encountered in the application of the Papanicolaou technique to urinary sediment are discussed Stringent criteria for positive interpretation are outlined.

The authors express appreciation to Drs. Alvin Cox, David Wood, Frederick Howard, Milton Rosenberg, Charles King and Eileen King for aid in the preparation of this paper.

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

THE EFFECT OF ACTH ADMINISTRATION ON THE URINARY EXCRETION OF ANDROGENS AND OTHER STEROIDS BY OLD MEN IN COMPARISON WITH YOUNG MEN: PRELIMINARY REPORT

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This is a progress report of a continuing study of the changes in endocrine status associated with increasing age in the adult human male. It is particularly hoped that studies of this nature may throw additional light on the etiology and rationale of therapy of cancer of the prostate and of the male breast. Previous publications from our laboratories[1–5] have reported the results of assays of the urinary steroids of patients with cancer of the prostate as affected by orchiectomy, adrenalectomy, and steroid therapy. In the present report, elderly men have been compared with young men, with respect to the effect of ACTH on the urinary excretion of 17-ketosteroids and 17-hydroxycorticoids, measured chemically, and of androgens measured by biological assay.

The decline in the urinary excretion of androgens and of total 17-ketosteroids with age has long been recognized. The pertinent literature has been reviewed by Dorfman,[6] Mason and Engstrom,[7] Hamilton[8] and Birke et al.[9] A study, recently reported by Dobriner,[10] in which the principal urinary steroids of 11 men under 50 and 9 men over 50 were individually quantitated, amply confirmed the earlier

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Read at annual meeting, American Association of Genito-Urinary Surgeons, Pebble Beach, Calif. May 23–25, 1955.

This work was supported in part by research grants (C-2051 and C-2056) from the National Cancer Institute of the National Institutes of Health, Public Health Service and by a Contract (N5 ori-76) between Harvard University and the Office of Naval Research.

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TABLE 1 *Comparative urinary excretion of 17 hydroxycorticoids 17 ketosteroids, and androgens by young men and old men*

	17 Hydroxycorticoids (mg /24 hrs)		17 Ketosteroids (mg /24 hrs)		Androgens (I U /24 hrs) Mean
	Mean	Range	Mean	Range	
9 young men, age, 19–30	5	1–11	[illegible]	11 38	62
9 old men, age, 65–87	6	2–14	[illegible]	4–13	12

studies based on less discriminating methods However the excretion of urinary steroids known to originate exclusively from adrenal cortical precursors was not found to differ significantly between the two age groups The question of possible differences in adrenal cortical activity related to age was re examined in a subsequent study by Dobriner[11] Here, no consistent differences in the effect of ACTH administration on urinary steroid patterns were found between two young men and two older men The wide differences between individuals, however, suggested that it might be necessary to investigate the question more extensively, using larger numbers of subjects, and in the present report observations on nine subjects in each age group form the basis for our conclusions

Extracts of acid-hydrolyzed urine were prepared and the 17-ketosteroids were determined by the method of Klendshoj et al[12] and androgens by a modification of the baby chick comb weight method of Rakoff et al ,[13] previously described[3] [14] 17-Hydroxycorticoids were determined by the method of Reddy et al[15]

RESULTS AND DISCUSSION

The nine young men used in this study were 19 to 30 years of age The nine older men were aged 65 to 87 years Two of the older men had been orchiectomized, one for cancer of the prostate, and the other for bilateral epididymitis, but these deviations from normality were not reflected in detectable abnormalities of steroid excretion All the subjects were in good health at the time of the urine collections

The mean values and ranges for the urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and androgens during control periods are shown in table 1 In confirmation of other investigators, the excretion of 17-ketosteroids and androgens was found to be definitely lower in the older group, although there was a slight overlap No significant difference in the excretion of 17 hydroxycorticoids between the two age groups was apparent, however

The effect of ACTH administration on steroid excretion, as influenced by age,

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TABLE 2. *Urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and androgens. Mean increase over control periods during 2-day period of administration of ACTH gel. Comparison of 5 old men with 5 young men*

	17-Hydroxycorticoids (mg /24 hrs)		17-Ketosteroids (mg./24 hrs)		Androgens (I U /24 hrs)	
	20 c u.*	80 c.u	20 c.u.	80 c.u.	20 c.u.	80 c u
5 young men; age, 20–30	8	20	6	19	no increase	28
5 old men; age, 65–87	9	32	2	20	no increase	12

* Daily dose of ACTH gel in clinical units.

TABLE 3. *Urinary excretion of 17-hydroxycorticoids, 17-ketosteroids, and androgens. Mean increase over control periods during 2-day period of administration of 25 U.S.P. units of ACTH by 8-hour intravenous infusion. Comparison of 4 old men with 4 young men*

	17-Hydroxy-corticoids (mg /24 hrs)	17-Ketosteroids (mg /24 hrs)	Androgens (I U./24 hrs)
4 young men; age 19–30	20	14	30
4 old men; age 65–76	10	11	8

was determined in two separate studies. In the first experiment, the responses of 5 young and 5 older men, all in possession of intact adrenals and testes, were compared. Control 24-hour urine specimens were collected on three consecutive days. ACTH in gelatin* was administered once daily for the 4 days immediately following, 20 clinical units on each of the first 2 days, and 80 clinical units for the final 2 days. The test was repeated on each man after an interval of two to three weeks. A summary of the results is shown in table 2. The rise in 17-ketosteroid excretion during ACTH administration was very similar in the two age groups, but, surprisingly enough, the rise in 17-hydroxycorticoid excretion by the older men was significantly greater than that of the young men, by statistical criteria. The rise in androgen excretion was detected only at the higher dosage level of ACTH, and was markedly greater in the young men than in the older men.

In the second experiment, 4 young men and 4 older men were administered ACTH† by 8-hour continuous intravenous infusion on two consecutive days. (Two of the older men had been orchiectomized, as noted above.) Control 24-hour urine collections were made for two to four consecutive days immediately preceding the administration of ACTH. The results are summarized in table 3. The results, with respect to the effect of age on the response to ACTH, were very similar to those of the first experiment, except in one particular, the smaller increase in excretion of 17-hydroxycorticoids by the older men as compared with that of the young men. The difference was statistically significant.

The effect of ACTH on the mean 17-hydroxycorticoid excretion by the young men was essentially the same in both experiments, in spite of the change in dosage, route and duration of administration, and nature of the ACTH preparation, the vagaries of the analytical procedure, and individual variation. The mean response of the older men, however, was much lower in the second experiment, in which ACTH was administered by intravenous infusion. Before accepting this unexpected result as conclusive and attributing it to the nature of the ACTH treatment, however, we feel that additional studies will be necessary.

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* "HP Acthar gel," all of a single lot, supplied gratis by the Armour Laboratory.

† Corticotropin, supplied gratis from the Research Laboratories of the Upjohn Company.

It has been demonstrated repeatedly that during ACTH administration the urinary excretion of 17-ketosteroids and 17 hydroxycorticoids increases markedly, and the data of the present report are in excellent agreement with studies by previous investigators. The increased excretion of androgens during ACTH administration, however, was first documented in [illegible] preliminary reports from our laboratories,[2, 4, 5] and these earlier observations have now been confirmed and extended by the new data.

Furthermore, it has now been demonstrated that the increase in androgen excretion, in terms of international units per 24 hours during ACTH administration, is much greater in young men than in elderly men. The percentage increase in androgen excretion during ACTH treatment over the control period was, nevertheless, greater in the older group. It is also of interest that the ratio of increase in androgens to increase in total 17 ketosteroids (I.U./mg.), was lower in the older group. It may be speculated that if ACTH administration were continued over a longer period of time, the androgen excretion of older men might approach that of young men.

In any event, these studies have demonstrated that older men can respond to ACTH administration by a considerably increased excretion of steroids, including androgens, although, with respect to androgens, perhaps not so promptly or vigorously as young men. The satisfactory explanation of differences in the excretion of 17-hydroxycorticoids between young and old men must await further investigation. Finally, it must be concluded that our data, thus far, are not in complete accord with the idea that the differences in adrenal steroid excretion between old men and young men are entirely the result of a decreased rate of secretion of ACTH in old men. The possibility remains that, in advanced age, the pattern of adrenal cortical secretion and the intermediary metabolic processes may also have undergone significant alteration.

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

THE BACTERIAL FLORA OF URINE SPECIMENS FROM NORMAL ADULTS

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There are inconsistencies in the literature regarding the diagnostic significance of bacteria found in urine properly collected for bacteriological examination. Gould states that "Organisms isolated on bacteriological examination are significant when the methods of collecting the urine are satisfactory and the technique of the laboratory is of high standard. Under these conditions, no organisms are isolated from the urine of healthy persons and patients who have no disease of the urinary tract." Kleinschmidt, on the other hand, reported that thirty-five (17 per cent) of 200 females studied were found to have bacteriuria not associated with urinary tract disease. Approximately one third of this group of thirty-five were completely healthy and asymptomatic in every respect. Lazarus stresses the importance of detailed bacteriological examination of urine requiring culture methods for species identification. Cook states, "The general practitioner as well as the specialist can satisfactorily examine, diagnose, and treat the great majority of the patients he sees by using Gram's stain of the urinary sediment to ascertain the general type of infection present."

All of the aforementioned authorities agree that urine from females should be obtained by the use of a sterile catheter and the three (Cook, Lazarus, Gould) who dealt with males agree that a midstream voided specimen from males after proper cleansing of the external genitalia is satisfactory. The differences in opinion, therefore, reflect variations in bacteriological technique and interpretation.

In order to establish a base line of normals that will aid in determining the diagnostic significance of bacteria in the urine and clarifying the above mentioned disagreements, a study has been made of the bacterial flora of urine fror 100 normal adults, 50 of which were male and 50 female.

PROCEDURES

The volunteers whose urine was studied varied in age from 18 to 67 y but the majority were between 20 and 30 years. Fourteen of the total n had mild symptoms of urinary tract disorder such as occasional burni urination or nocturia, but none of them were sufficiently annoyed to seek ical attention or to alter their daily routine of activities. The remainde were found to be completely free of symptoms of urinary tract diseas careful questioning and were actively engaged in employment.

Procedure for collecting urine samples from males was as follows:

1) The foreskin was reflected backwards and the glans penis rin water.

Accepted for publication July 26, 1955.

This work was done with the help and advice of W. D. Stovall, M.D., D Ph.D., and Miss Ann Knell, and other members of the staff of the Universit

2) The glans was washed carefully with tincture of green soap and a sterile sponge, and rinsed with a 1–5000 aqueous solution of potassium mercuric iodide At this point the penile meatus of 21 volunteers was swabbed with a sterile cotton applicator which was then immersed in 1 per cent lactose broth and incubated at 37°C The cultures were examined at periods of 24 and 48 hours after inoculation

3) From 30 to 100 cc of urine was voided and discarded Approximately 30 cc of bladder urine was then collected in a sterile container and cultures started within two hours

All specimens from males were collected by the author to ascertain that standard methods were observed in each case

The procedure of collecting samples from females was as follows

1) Using sterile rubber gloves the labia were spread apart exposing the external urethral orifice

2) The exposed area was washed with a sterile sponge and tincture of green soap (diluted 1.4 in sterile water to avoid irritation) and rinsed with a 1–5000 aqueous solution of potassium mercuric iodide

3) A sterile (autoclaved) rubber catheter was inserted into the bladder and approximately 30 cc of urine collected in a sterile container Cultures were started within 2 hours

All specimens from females were collected by one well qualified graduate nurse who used the same procedure on all volunteers

One ml of each urine sample was placed in a pour plate with Bacto plate count agar containing yeast extract, glucose, and tryptose, and buffered at pH 7 2 Ten ml of each urine sample were centrifuged at 3,000 r p m for 10 minutes and the residue examined for cellular content and stained by Gram's method for bacteria In addition, a loopful of the sediment of centrifuged urine specimens from males was placed in 1 per cent lactose broth with brom thymol blue indicator and another loopful streaked out on a blood agar plate Initial agar plate cultures were incubated at 37°C for 24 to 28 hours Lactose broth was held for a total of 48 hours before it was considered negative

The term, Micrococcaceae refers to the family of bacteria that includes the genera Micrococcus (Staphylococcus), Gaffkya, and Sarcina These organisms were identified on the basis of colonial morphology on a blood agar plate and cellular morphology after Gram staining

All streptococci recovered were placed in 1 per cent glucose broth overnight and transferred to 6 5 per cent sodium chloride broth at pH 7 2 Organisms growing on the latter medium were classified as enterococci Streptococci that failed to grow in 6 5 per cent sodium chloride broth were classified on the basis of hemolysis on a blood agar plate

Gram negative rods that ferment 1 per cent lactose broth were classified as members of the genus Escherichia or Aerobacter The two strains of gram-negative Bacterium anitratum were identified on the basis of the characteristic fermentation reactions particularly their ability to ferment 10 per cent lactose, but not 1 per cent lactose

TABLE 1. *Number of urine specimens from 100 normal volunteers showing bacteria by various techniques*

Method	Specimens from 50 Males Showing Bacteria		Specimens from 50 Females Showing Bacteria	
	Number	% of total	Number	% of total
1. Plate count agar 1–30 colonies/cc.	27	54	14	28
30–400 colonies/cc	10	20	3	6
Over 400 colonies/cc	4	8	0	0
Total	41	82	17	34
2. 1% lactose broth	26	52	not done	not done
3. Blood agar streak plate				
Less than 16 colonies per plate	11	22	not done	
Over 16 colonies per plate	1	2		
Total	12	24		
4. Gram stain	1	2	2	4

RESULTS

As shown in table 1, 82 per cent of midstream urine specimens from 50 apparently normal males showed bacteria, when 1.0 cc of undiluted urine was cultured in a pour plate with plate count agar. Only 28 per cent showed more than 30 organisms per cubic centimeter and the highest number found in a single specimen was 5,700. This figure can be regarded as only an approximation since accurate plate counts of bacteria can be obtained only when the number of bacteria is within the range of 30–400 per plate.

Using a loopful of centrifuged urine as an inoculum, bacteria were recovered from 52 per cent of urine specimens from males cultured in 1 per cent lactose broth, and from only 24 per cent of specimens streaked on a blood agar plate. The single specimen containing bacteria revealed by Gram's stain of centrifuged urine was the one showing approximately 5,700 organisms per cubic centimeter. Organisms seen by direct examination of uncentrifuged urine are probably present in numbers of 100,000 per cubic centimeter or greater.

Table 1 also shows that a catheterized urine specimen from a normal female is much more likely to be sterile than is a midstream specimen from a normal male. By the most sensitive method of detecting bacteria (plate count) only 34 per cent of urine specimens from females contained bacteria in contrast to 82 per cent from males. The average number of bacteria per cubic centimeter from females is also significantly less than that from males. On direct microscopic examination of centrifuged urine from females, bacteria were seen in only 2 of the 50: gram-positive cocci in one and gram-positive bacilli in the other. Neither of these organisms grew on plate count agar indicating that although it was the most sensitive of the media used in these experiments, plate count agar is by no means a perfect medium for the growth of all bacteria.

The organisms recovered from "normal" urine listed in table 2 include many

TABLE 2. *Number of urine samples from 100 normal volunteers showing various types of bacteria*

Type of Bacteria	Males (Total 50)		Females (Total 50)	
	No. of specimens	% of total	No of specimens	% of total
Beta hemolytic streptococci	0	0	1	2
Alpha hemolytic streptococci	0	0	2	4
Micrococcaceae	22	44	9	18
Enterococci	1	2		
Escherichia-Aerobacter	2	4		
Micrococcaceae + Escherichia-Aerobacter	1	2		
Micrococcaceae + paracolon	1	2		
Micrococcaceae + Alpha hemolytic streptococci	4	8	1	2
Micrococcaceae + Beta hemolytic streptococci	1	2	1	2
Micrococcaceae + diphtheroids	1	2	3	6
Micrococcaceae + Gram positive bacilli	1	2		
Micrococcaceae + Bacterium anitratum	2	4		
Micrococcaceae + enterococci	5	10		
Total	41	82	17	34

of those capable of causing disease of the genitourinary tract. Bacteria most frequently found were Micrococcaceae, a family that includes staphylococci and gram-positive cocci occurring in packets or tetrads frequently referred to as "micrococci." Although Goldstein reported that micrococci were not capable of producing experimental renal lesions in rabbits, Munger states, "The micrococci may in themselves produce a pyuria which picture, both objectively and subjectively, will rapidly be relieved under a few injections of neoarsphenamine." Detailed classification of staphylococci has not been done since the pathogenicity of these organisms is not necessarily related to pigment production, hemolysis, or results of the coagulase test. Levine considers the coagulase test to be the most significant of the three methods. Other types of organisms isolated in this series: Enterococci, alpha and beta hemolytic streptococci, Bacterium anitratum, and members of the genus Escherichia or Aerobacter (often referred to as coliform organisms or the "coliaerogenes group"), have all been reported as the cause of genitourinary tract infection.

Table 3 shows that cotton swabs of 19 of a total of 21 penile meatuses taken immediately after thorough cleansing and rinsing with disinfectant showed bacteria. Many of these organisms are potential pathogens of the urinary tract, and in 9 of the 21 volunteers the same organisms were isolated from urine that were cultivated from meatal swabs.

Only 2 of the 100 urine specimens examined showed abnormal cellular content on direct microscopic examination after centrifugation. Both were from males; one showed 15–20 white blood cells per high powered field; and the other 15–20 red blood cells per high powered field. There was no correlation between these findings and bacteriuria or the slight symptomatology mentioned under Procedure. The man whose urine contained 5,700 organisms per cubic centimeter was completely asymptomatic and the cellular content of his urine was normal.

TABLE 3. *Correlation of bacteria found in urine and meatal swabs from 21 normal males*

Bacteria Found in Urine	Bacteria Found on Meatal Swabs	No of Volunteers
Micrococcaceae	Micrococcaceae	6
No growth	Micrococcaceae	3
Micrococcaceae + Bact. anitratum	Micrococcaceae	2
No growth	No growth	1
Micrococcaceae + A. hem. Strep.	B. hemolytic streptococci	1
Micrococcaceae	Gram-positive bacilli	2
Micrococcaceae + A. hem. strep.	Micrococcaceae	1
Micrococcaceae	No growth	1
Enterococci	Enterococci	1
Escherichia-Aerobacter	Escherichia-Aerobacter	1
Micrococcaceae + B. hem. strep	Micrococcaceae + B. hem. strep	1
No growth	Gram-positive bacilli	1

DISCUSSION

The variations in sensitivity of the four methods listed in table 1 for detecting the presence or absence of bacteria in urine can be explained at least partially on the mechanics of handling the urine. Ordinary glass centrifuge tubes have been broken in this laboratory when spun at speeds greater than 3,000 r.p.m. It is doubtful that at this speed for a period of 10 minutes all the bacteria present in 10.0 cc of urine will be completely sedimented.

Even if one assumes, however, that all the bacteria present in the original specimen are concentrated in the sediment, other factors still must be taken into consideration. The usual procedure in most laboratories is to decant the supernatant fluid leaving approximately 0.2–0.5 cc of sediment. A platinum loop measuring 5 mm. in diameter will transfer approximately 0.003 cc of water. Depending upon such variable factors as viscosity of urinary sediment and the angle at which the loop is held, an ordinary platinum loop may not transfer more than .003/.2 or 1.5 per cent of the bacteria contained in the original urine sample. One cubic centimeter of uncentrifuged urine will, on the other hand, contain 10 per cent of a 10.0 cc sample. Bacteria adhering to the platinum loop are much more likely to be removed when immersed into a liquid broth than when one side of the loop is streaked on a solid agar plate. Therefore, even if the nutritional factors of all media are the same, methods employing 1.0 cc of uncentrifuged urine should be more likely to reveal bacteria, than methods employing a loopful of centrifuged urine and when the latter method is employed liquid media should reveal a higher percentage of positives than solid. Variations in methodology probably account for some of the discrepancies in the literature. The overwhelming majority of specimens reported herewith would undoubtedly have been "sterile" if only a loopful of uncentrifuged urine had been streaked on a blood agar plate.

The present work is consistent with that of Levine who reported, "it is evident that the presence of staphylococci both coagulase positive and coagulase negative, on all media is associated in most cases with leukocytes and erythrocytes in the urine We see that both the coagulase positive and negative strains when on liquid media alone, are associated with few or no leukocytes or erythrocytes in the urine as well as with few cases of albuminuria " Levine inoculated a loopful of urine on 5 per cent human blood agar and eosin methylene blue agar while he placed 0 5–1 0 cc in liver peptone broth The latter method is much more likely to reveal presence of bacteria in small number than is the method for inoculating the two solid media

McClane and Trout[8] studied the urine of 30 obstetrical patients during various stages of their antenatal and puerperal periods Of 115 catheterized urine specimens obtained from the right ureter of these patients, 15 per cent showed bacteria and of 58 specimens of bladder urine, 55 per cent showed bacteria Since the ureteral urine was plated directly on an ascitic agar slant and the bladder urine (the amount was not stated) was cultured in beef infusion broth, the variations in the percentage of specimens in the two groups showing bacteria may be due to variation in technique rather than source from which urines were derived

The species Bacterium anitratum was described in 1948 by Schaub and Haubinger as a gram-negative, nonmotile rod capable of fermenting 10 per cent lactose, glucose, and galactose It does not ferment 1 per cent lactose or other carbohydrates used in the identification of gram-negative bacilli Schaub and Haubinger isolated this organism from nine urine specimens, five of which were from individuals known to have genitourinary tract infection Histories were not available on the other four Bacterium anitratum was also found in pleural fluid, pericardial fluid, heart blood, lungs, and cervix The demonstration of this organism in urine from two normal individuals emphasizes that its isolation from urine is not *per se* diagnostic of infection

It is not known whether the bacteria isolated from the urine of normal individuals comes from the urinary tract or represents contaminants from the external urethral orifice Table 3 shows that the meatus of the male penis has not been sterilized by the cleansing operation employed prior to the voiding of urine

Seastone reported that saline washings of the hands cleansed with the best available surgical techniques contain bacteria It is not likely that the glans penis can be more easily sterilized than human hands and urine passing through a contaminated meatus is just as likely to contain bacteria as is saline passing over contaminated hands The correlation of bacteria found on the meatus with that found in the urine further suggests contamination Morse reports that Corynebacterium renale, a causative agent of infectious cystitis and pyelonephritis of cattle, was isolated from the urine of 17 6 per cent of 523 apparently normal dairy cattle Vaginal or penile swabs of 108 normal cattle made immediately after slaughter proved positive for C renale in 4 instances, but no diphtheroid bacilli were isolated from the bladder urine

Regardless of whether the bacteria reported herewith represent contaminants or inhabitants of the genitourinary tract, the fact that they were present in a certain per cent of urine samples collected from apparently healthy individuals by methods widely accepted as satisfactory, must be recognized in the clinical interpretation of urine cultures. The length of time and temperature of the storage of these specimens must also be considered.

SUMMARY AND CONCLUSIONS

Bacteria were found in 82 per cent of 50 midstream voided specimens from normal human males and 34 per cent of 50 catheterized specimens from normal human females when 1 cc of urine was placed in a plate count agar pour plate.

When a loopful of centrifuged urine was placed in 1 per cent lactose broth, 52 per cent of the specimens from males showed bacterial growth and only 22 per cent were positive when a loopful of centrifuged urine was streaked on a blood agar plate.

Bacteria were seen on Gram's stain of centrifuged urine from one of the 50 specimens from males and two from females.

Many of the types of bacteria isolated have been reported as pathogenic for the genitourinary tract.

It is concluded that the demonstration of potentially pathogenic bacteria in a properly collected urine sample is not in itself diagnostic of infection. Since bacteria in most of the urine samples studied in this series were present in small numbers, the bacteriologist may be of additional aid to the clinician by giving him some idea of the number of bacteria present in a given sample of urine within a specified time limit as well as identifying species and determining sensitivities. Direct microscopic examination of urine stained by Gram's method is of considerable value in this regard since bacteria seen in uncentrifuged urine by this procedure are probably present in numbers of 100,000 per cubic centimeter or greater.

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THE JOURNAL OF UROLOGY
Vol 75 No 3 March 1956
Printed in U S A

AIR EMBOLISM DURING PRESACRAL PNEUMOGRAPHY A CASE REPORT

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Since Ruiz Rivas' original paper on presacral pneumography in 1950, this method has increased in popularity[1] A number of reports have appeared in the literature describing the many advantages of this technique, including its safety Thus, Blackwood[2] noted only transient lumbosacral discomfort and distention among his patients Similarly, Tinckler,[3] Steinbach[4] and others have reported their experiences without any significant complications

The purpose of this paper is to record the occurrence of air embolism resulting from presacral air injection A similar accident, also with recovery, was reported recently by Russ, Glenn and Gianturco[5] One death due to air embolism was mentioned in passing by the editors of *The Year Book of Radiology*[6]

The possibility of air embolism is ever present with this diagnostic procedure and must be appreciated The pertinent anatomic features to be considered are as follows[7] The hemorrhoidal veins form an intertwining plexus about the rectum and anterior sacrum The middle sacral veins, in particular, traverse the anterior sacral wall more or less in the midline to anastomose with the hemorrhoidal plexus Similarly, the middle sacral artery, which arises at the bifurcation of the aorta, courses in the midline along the anterior surface of the sacrum It is possible to enter these presacral vessels with a midline puncture The lateral sacral veins, which arise from the hypogastric vein, accompany the lateral sacral arteries along the anterolateral aspect of the sacrum These vessels are less likely to be entered unless the puncture is made quite laterally See figure 1

CASE REPORT

I R, a 70 year old white man, was admitted to the Hospital of St Raphael on October 28, 1954 for further study of a left abdominal mass On November 9, 1954, a presacral air study was performed With the patient in the knee chest position, a No 20 three inch spinal needle was introduced into the left buttock approximately five centimeters lateral and two centimeters superior to the tip of the coccyx The point of the needle was advanced until it reached the anterior

Accepted for publication July 20, 1955

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[2] Blackwood, J Presacral perirenal pneumography Brit J Surg, 39 111-119, 1951

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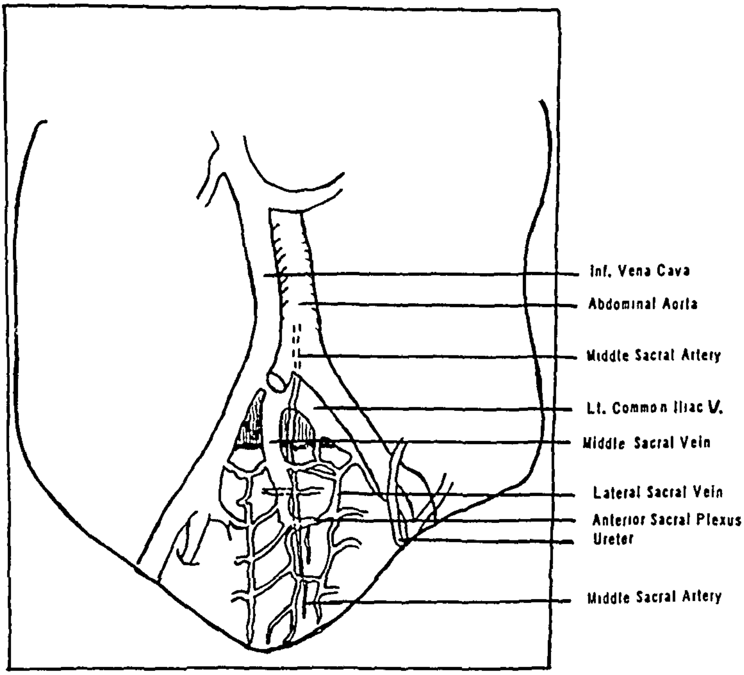

FIG. 1. Sacral vascular distribution

sacral wall whereupon it was withdrawn several millimeters. Preliminary aspiration yielded no blood. Three hundred cubic centimeters of air were injected without difficulty. At this stage the patient became cyanotic, complained of chest pain, and exhibited stertorous respirations and a feeble pulse. He was immediately placed in the left lateral decubitus position to prevent circulatory obstruction due to an air trap in the right ventricular outflow tract. Ausculation of the heart disclosed an arrhythmia but no characteristic "swishing" sound.

The patient's condition improved considerably. An additional 300 cc of air were introduced into the presacral space with the patient in the semi knee-chest position. The patient then lapsed into an unresponsive state. He was placed in the left lateral decubitus position again and given O_2 by mask. Thirty minutes later his blood pressure was 80/60 but his pulse was full and regular. Physical examination disclosed paralysis of the right upper extremity and left facial weakness. Oxygen therapy was continued until his condition was improved and he was transferred to his room.

The patient remained semicomatose over the course of the subsequent 12 hours during which period he had recurrent generalized seizures which predominately involved the left side of the body. Recovery of the paralysis of the right upper extremity took place within several hours. On the following day, however, there was evidence of horizontal nystagmus and diffuse weakness of the left upper extremity. Flame-shaped hemorrhages were noted in the left optic fundus and several petechiae were evident in the left lower conjunctival sac. Over the course of the subsequent five days there was progressive subsidence of the nystagmus and recovery of motor power in the left upper extremity. His sensorium cleared satisfactorily and there were no subsequent seizures X-rays of the skull failed to disclose evidence of bony abnormality or shift in the pineal gland Later in his hospital course, a suprapubic cystotomy was performed for chronic urinary retention secondary to benign hypertrophy of the prostate gland The patient was discharged from the hospital on December 2, 1954, his thirty-fourth hospital day

SUMMARY

A case of air embolism complicating presacral pneumography is reported The significant anatomical data pertaining to this accident are reviewed

THE JOURNAL OF UROLOGY
Vol. 75, No. 3, March 1956
Printed in U.S.A.

NEPHROGRAPHY DURING ROUTINE EXCRETORY UROGRAPHY

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The purpose of this paper is to describe a method of obtaining a nephrogram during routine excretory urography by exposing an 11 by 14 inch film at the proper time. A rapid injection (10–15 seconds) of a highly concentrated organic iodine compound (urokon 70 per cent) makes this possible. The technique has been used in 195 cases without serious untoward reaction. It is the author's belief that it is a safe and practical method for routine excretory urography in the private office or hospital x-ray department and the method is presently being used at the United Hospital.

Precedents for this study are as follows: Nesbit and Nesbitt[1] have shown that the intravenous injection of 25 cc of urokon 70 per cent in 585 cases produced mildly annoying side reactions which were no greater in incidence than those encountered with other medications though greater than encountered with urokon 30 per cent. They believed that the tremendous improvement in pyelogram quality overcame the objectional features of the side reactions and "are now using urokon 70 per cent exclusively for pyelography at University Hospital," (University of Michigan). Barry and Rose[2] report that in 1160 cases by using urokon 70 per cent and rapid injection (usually 15–20 seconds) there was "a greatly decreased toxic reaction over that of any other medium now employed." Porporis et al.[3] used urokon 70 per cent with as rapid an injection as possible using an 18 gauge needle in 2500 routine intravenous pyelograms and found that better urograms resulted than previously obtained with less concentrated iodinated compounds. Robb and Steinberg[4] first noted demonstration of the renal parenchyma after intravenous administration of organic iodine compounds. Weens et al.[5] described a method of intravenous nephrography using 50 cc of diodrast 70 per cent solution and a rapid (2 second) injection through a special 12 gauge needle. They performed 35 such examinations and noted opacification of the kidneys beginning in 9 to 12 seconds after injection. Vesey et al.[6] described an intravenous method of nephrography in which opacification of the renal outlines was ob-

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Accepted for publication September 21, 1955.

[1] Nesbit, R. M. and Nesbitt, T. E.: Experiences with high concentration urokon for pyelography. Univ. Mich. Med. Bul., **18:** 225–231, 1952.

[2] Barry, C. N. and Rose, D. K.: Urokon sodium 70 per cent in excretory urography. J. Urol., **69:** 849, 1953.

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tained by appropriately timed films following the injection of large doses of concentrated organic iodine-containing contrast substance. Their method consisted of a very rapid injection (less than 2 seconds) of neo-iopax 75 per cent or diodrast 70 per cent using a 12 gauge Robb-Steinberg needle, films at 6 to 20 seconds after injection, and a second film as soon as the cassette could be changed (usually within less than 10 seconds). Wall and Rose[7] reported an intravenous technique using 50 cc of urokon 70 per cent injected in 5 seconds with a 15 gauge needle and taking films at approximately 10 and 25 seconds. In 80 cases they obtained opacification of the renal parenchyma in each instance. Wall and Rose placed the x-ray tube and film so that the patient's kidneys (rather than the entire urinary tract) were centered. Porporis et al.[3] mentioned without further elaboration that "25 cc of urokon 70 per cent provided a moderate degree of opacificaton of the renal shadows. . . ."

Thus it has been shown that a rapid injection of 25 cc of urokon 70 per cent is safe and produces pyelograms of good to excellent quality, and that appropriately timed films taken after the injection of 25–50 cc of urokon 70 per cent demonstrate opacification of the renal parenchyma.

To determine the practicability of nephrography as a part of routine intravenous pyelography the present study was undertaken.

METHOD

The following technique has been used.

The patient is given a cathartic the evening before the examination. For this purpose castor oil, licorice powder, or saline cathartics are prescribed depending upon the preference of the referring physician. A light supper is allowed.

Foods and liquids are withheld from 9 p.m. of the evening prior to the examination until the examination is completed.

Pyribenzamine 100 mg. or similar antihistaminic is given orally approximately 2 hours prior to the examination.

A preliminary 14 by 17 inch film is taken with the patient in Trendelenburg position. No compression is used.

A sensitivity test is performed by injecting ½ cc of urokon 70 per cent solution intravenously. The patient is then observed for a 10-minute period.

During the 10-minute waiting period the preliminary film is checked for radiographic technique and placement. The x-ray tube is centered on an 11 by 14 inch cassette, placed crosswise under the kidney area.

If there is no untoward reaction to the test dose, 25 cc of urokon 70 per cent is injected intravenously using an 18 gauge needle, in 10 to 15 seconds. Venipuncture technique must be meticulous because extravasation of urokon 70 per cent could produce pain and local tissue reaction.

The injection is timed and at 30 seconds from the beginning of the injection the nephrogram film is exposed.

At 2 to 3 minutes the patient is given a cup of water (about 4 oz.). This is believed to produce better filling of the renal collecting system and ureters in subsequent films.

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[7] Wall, B. and Rose, D. K.: The clinical intravenous nephrogram: Preliminary report. J. Urol., 66: 305–14, 1951.

At 5 minutes the first pyelogram in the series is taken on an 11 by 14 inch film placed like the nephrogram film. Ten- and 15-minute conventional 14 by 17 inch pyelogram films are exposed, and an upright film is taken at 20 minutes.

The 10-minute film is inspected before the examination is considered completed and additional oblique, lateral, or delayed films ordered as indicated.

RESULTS

The above described method was used during 100 intravenous pyelograms performed on consecutive unselected cases at United Hospital. Nephrogram films were taken variably at 30 seconds, 60 seconds, and at 2 minutes during the first 100 cases. The 30-second film was found to be by far the most satisfactory. In subsequent examinations only the 30-second film has been taken. The films obtained in the first 100 cases using the "routine nephrogram" technique were reviewed by the author and by a urologist. The nephrograms were classified as to quality using the following criteria:

1) None: No discernible opacification of the renal shadows.

2) Poor: Slight opacification of the renal shadows but not sufficient to clearly demonstrate the renal outlines. There was no increase in renal density when compared with subsequent intravenous pyelograms.

3) Good: Definite opacification with clear delineation of renal outlines. The density of the renal shadows in this group was greater than the renal density in the preliminary film and in all subsequent pyelogram films.

4) Excellent: Opacification is equal to that obtained by the 50 cc urokon 70 per cent—2-second injection method.

Table 1 is a summary of the quality of nephrograms obtained by this method. The results indicate that in 64 per cent of cases a nephrogram was obtained in which the kidneys were significantly opacified and clearly outlined, providing information to the radiologist and urologist which would not otherwise be available from the pyelographic examination. Examples of 30-second routine nephrograms are shown in figures 1 and 2, in which scout films of the abdomen and nephrograms are compared. The quality of pyelogram was judged by the criteria of Nesbit:[4] "The pyelograms are rated Poor, Fair, Good, and Excellent. *Poor* quality films are those in which no satisfactory secretion of contrast medium is shown. *Fair* refers to a film showing visible excretion but no basis for a definite diagnosis other than obstructive uropathy. *Good* refers to satisfactory pyelo-

TABLE 1. *Quality of nephrograms obtained in 100 cases of "routine nephrogram during intravenous pyelography"*

None	6
Poor	30
Good	64
Excellent	0
Total	100

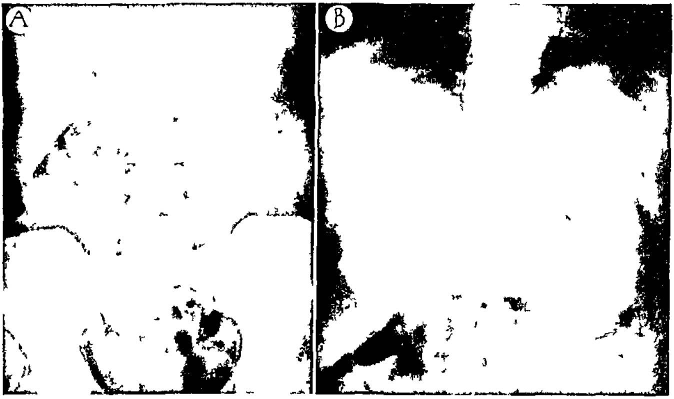

Fig 1 A, X ray of abdomen showing poor definition of renal outlines B, 30 second nephrogram of same patient demonstrating good opacification and clear outlines of kidneys

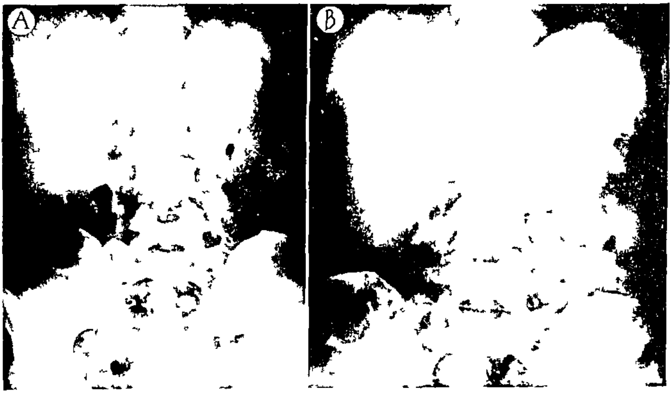

Fig 2 A, X ray of abdomen Renal outlines are partly visible B, 30 second nephrogram Kidneys well opacified and clearly outlined

Table 2 *Pyelographic quality obtained in 100 cases using 25 cc of urokon 70 per cent*

Rating	Urokon 70% Current Series—100 cases	Nesbit's Series	
		Urokon 70%—585 cases	Urokon 30%—1000 cases
Poor	2	7	11
Fair	30	14	25
Good	50	45	64
Excellent	18	34	

TABLE 3. *Reactions and effects of injection (10–15 second injection) of 25 cc of urokon 70 per cent in 100 cases in order of frequency of occurrence*

	No. cases
Sensation of warmth	72
Tingling sensation, mouth or elsewhere	45
Flush	40
Metallic or bitter taste	31
Nausea	21
Arm pain, slight	6
Urticaria	4
Sensation of voiding	3
Vomiting	2
Faintness or dizziness	2
Tachycardia	1

grams which make possible a definite opinion regarding diagnosis, and *Excellent* denotes a quality equal to that seen in satisfactory retrograde pyelograms."

The results of this series, table 2, are roughly comparable to those of Nesbit, and the pyelogram quality in general was superior to that previously obtained with less concentrated media.

REACTIONS

No serious reactions were encountered following the rapid injection of 25 cc of urokon 70 per cent solution. To date urokon 70 per cent has been used for a total of 195 pyelograms. The effects of and reactions to the injections are summarized in table 3. It should be noted that it was usual for the patients to notice certain sensations following the injections, e.g., a sensation of warmth, tingling in the mouth, throat, etc. True reactions were much less frequent, nausea resulting in 21 per cent of cases, vomiting in 2 per cent and urticaria in 4 per cent. In all cases of urticaria there was prompt clearing following intracutaneous use of 2–3 minims of epinephrine. The nausea and vomiting were always of short duration, lasting up to 1 to 2 minutes.

Oral antihistaminics were used prior to the injection of urokon 70 per cent in an attempt to prevent serious reactions to the drug and to decrease the incidence of minor reactions. However it is not the purpose of this paper to discuss the effectiveness of the use of antihistaminics.

DISCUSSION

A method is described for obtaining nephrograms as a part of routine excretory urograms. The results indicate that good nephrograms were obtained in 64 per cent of cases. The nephrograms were not so good as those obtained following use of 50 cc of urokon 70 per cent via a 12 gauge Robb-Steinberg syringe and needle, a 2-second injection and films timed to the patient's circulation time. However, the latter method is time-consuming and requires extra technical help and is not practical for routine use. The technique of routine nephrography has been kept as simple as possible, requiring no more time, contrast material, or technical help than a routine intravenous pyelogram.

The routine nephrogram method is not intended to replace the more complicated nephrogram technique. Its purpose is to increase the scope of the excretory urogram. It is conceivable that the method can be improved by taking a nephrotomogram rather than a nephrogram at 30 seconds. Evans[8] has described the technique of nephrotomography and feels that the nephrotomogram is much more useful than the simple nephrogram, provides clearer definition of renal pathology and frequently enables the differentiation of renal cysts from neoplasms. It is conceivable that this will be possible with nephrotomograms done at 30 seconds as part of routine excretory urograms and studies along this line are recommended.

SUMMARY

A method is described whereby good nephrograms were obtained in 64 per cent of 100 cases, during routine excretory urography.

The method essentially consists of a rapid (10–15 second) injection of 25 cc of urokon 70 per cent via an 18 gauge needle, a nephrogram film at 30 seconds, and conventional intravenous pyelogram films at 5, 10 and 15 minutes.

The method provides added information about the status of the renal parenchyma and is recommended as a routine procedure.

The author wishes to thank Dr. Dovell N. Bonnett, Greenwich, Connecticut for reviewing the films which are the subject of this report and for his helpful criticism and comments.

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[8] Evans, J. A., Dubilier, W. and Monteith, J. C.: Nephrotomography. Am. J. Roentgenol. & Rad. Ther., 71: 213, 223, 1954.

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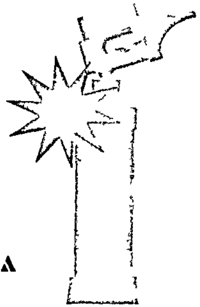
Western—Sheraton-Palace, San Francisco, April 30–May 3, 1956

Note by editor. A complete list of the executive committees of the various sections, and a complete list of the officers and members of the executive committees of the various branch societies was printed in the December 1955 issue.



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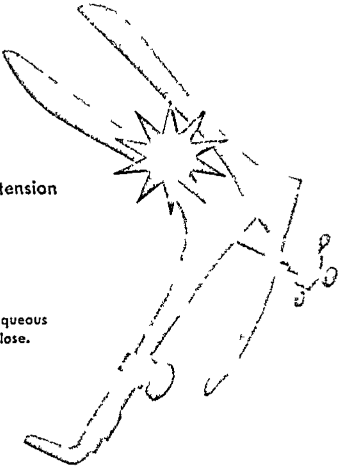

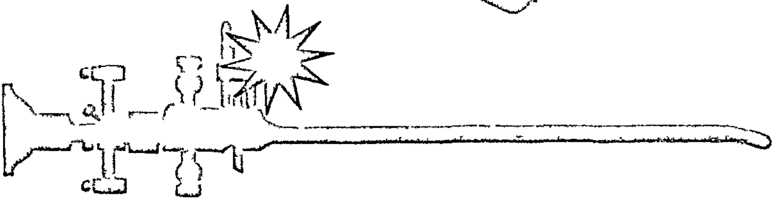

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The section on Perineal Prostatectomy has been rewritten by Dr. Albert E. Goldstein with new illustrations. In Chapter XXXVI more attention is given the problem of stress incontinence, and operations found beneficial in the author's experience have been added. Some changes have been made in many of the remaining chapters, consisting chiefly in the addition of surgical procedures or illustrations. A separate chapter has been added dealing with postoperative incontinence of the male.

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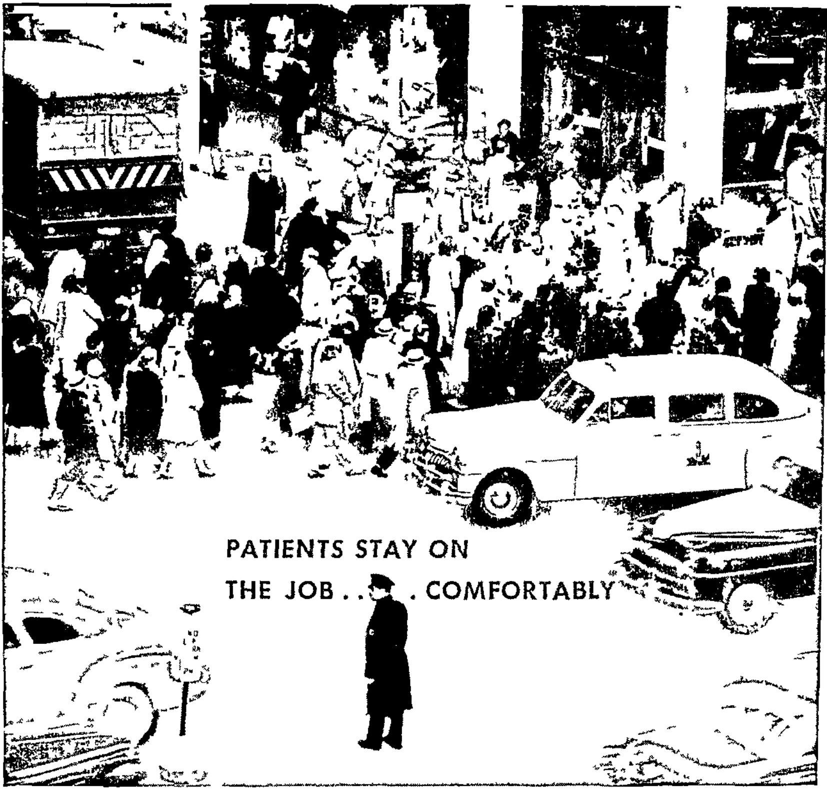

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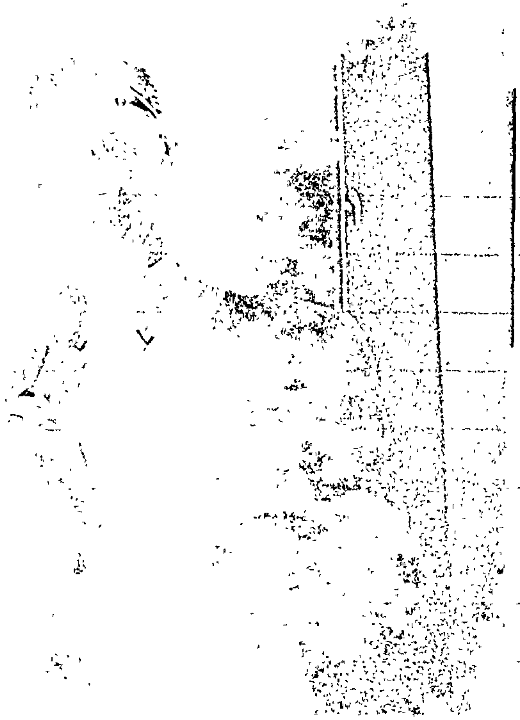

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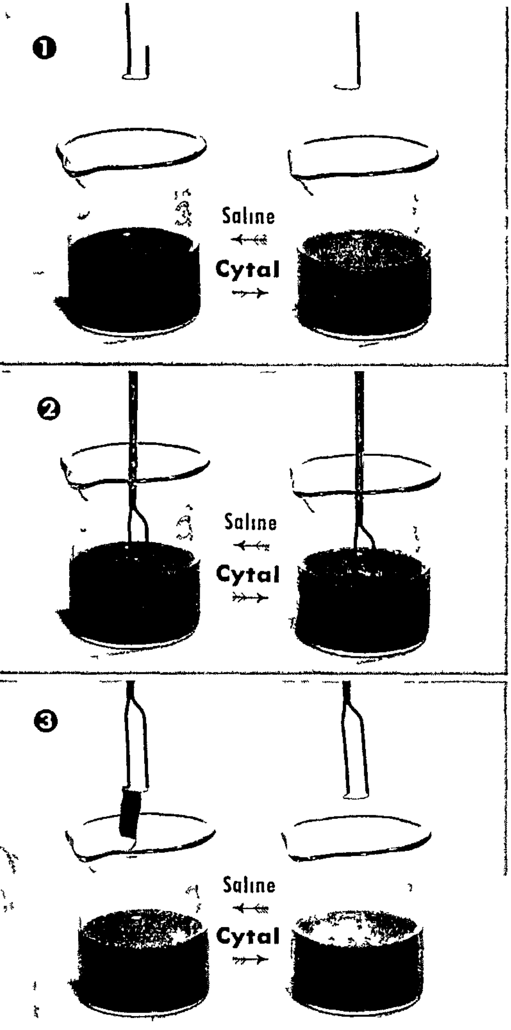

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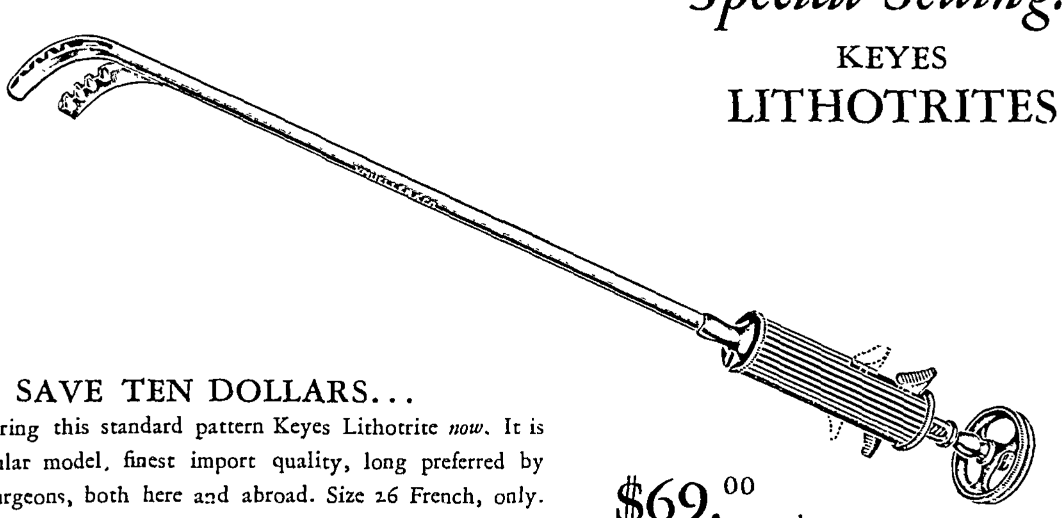

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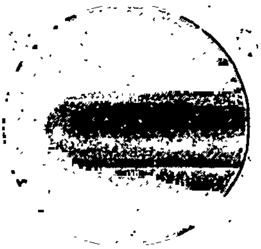

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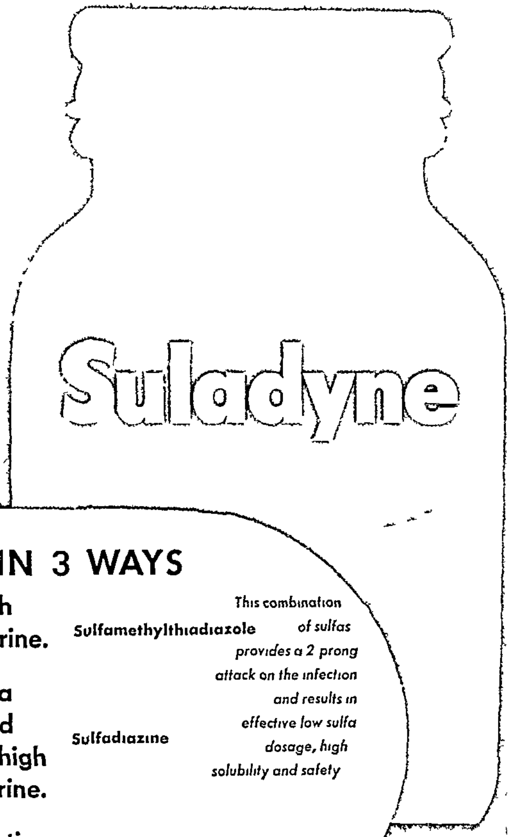

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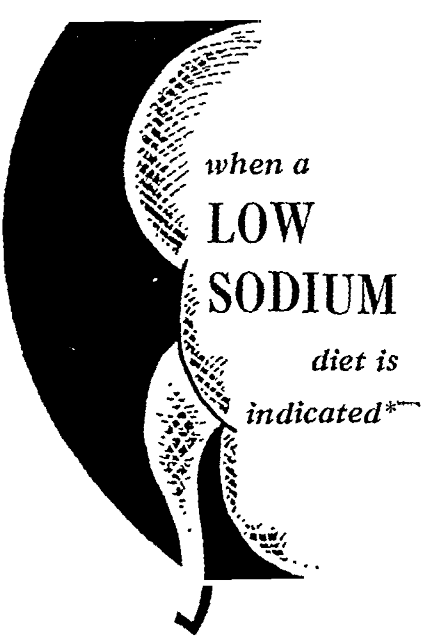

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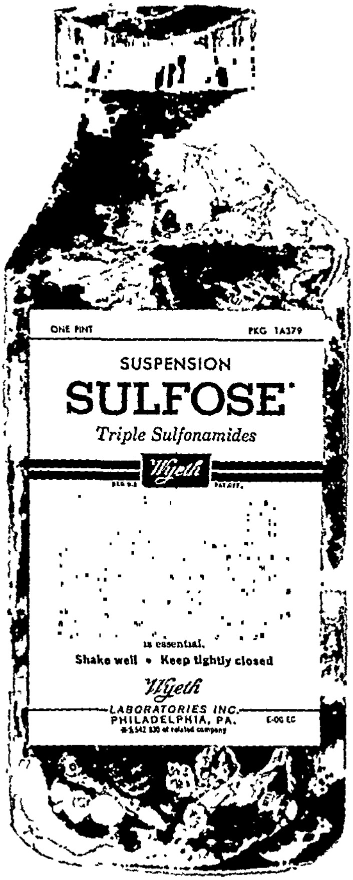

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Effect of ACTH Administration on Urinary Excretion of Androgens and Other Steroids by Old Men in Comparison with Young Men. *D. A. MacFarlane, C. B. Leman, P. L. Munson and J. H. Harrison* 558

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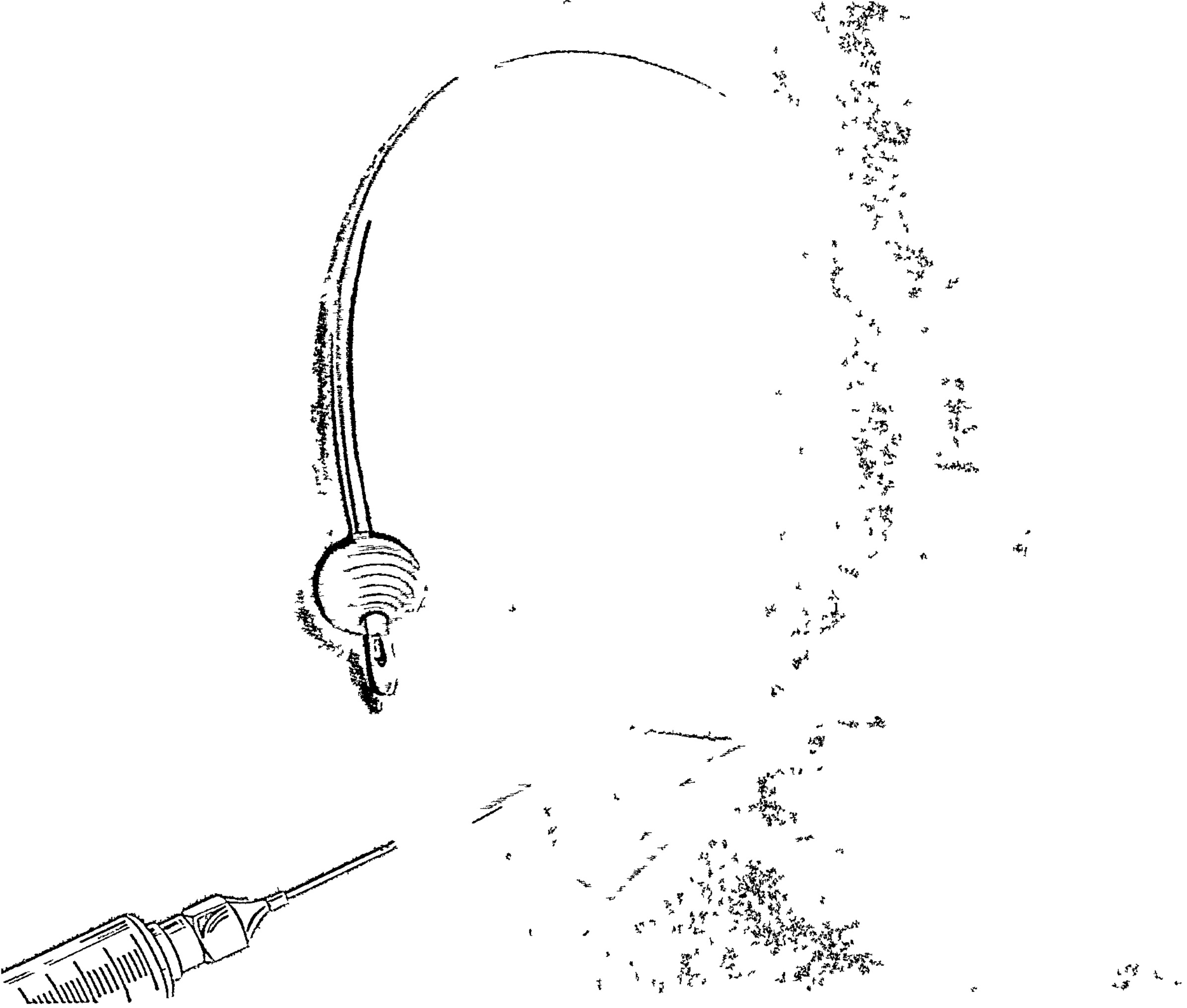

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1. Prien, E L., and Walker, B. S. J A M A. 160 355, 1956.
2. Prien, E. L., and Walker, B. S: J. Urol. 74 440, 1955; abstracted in J.A.M.A. 159:1575, 1955.
3. Prien, E. L., and Walker, B. S: New England J. Med. 253:446, 1955.

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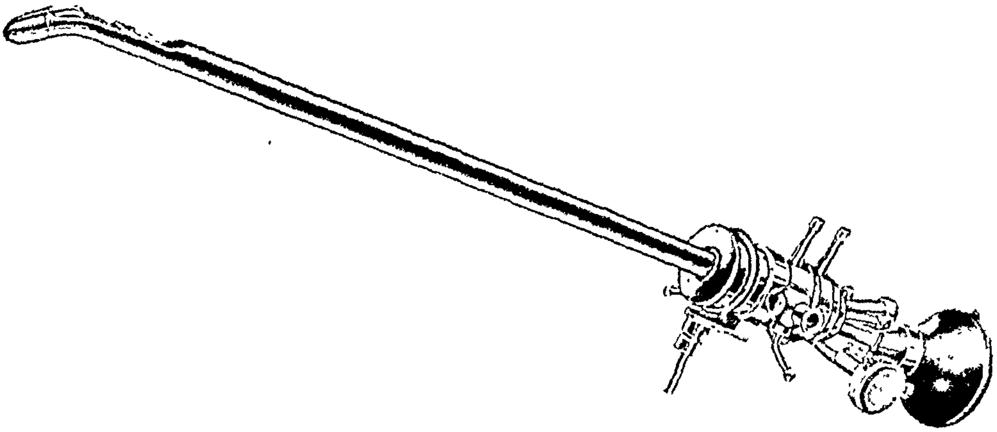

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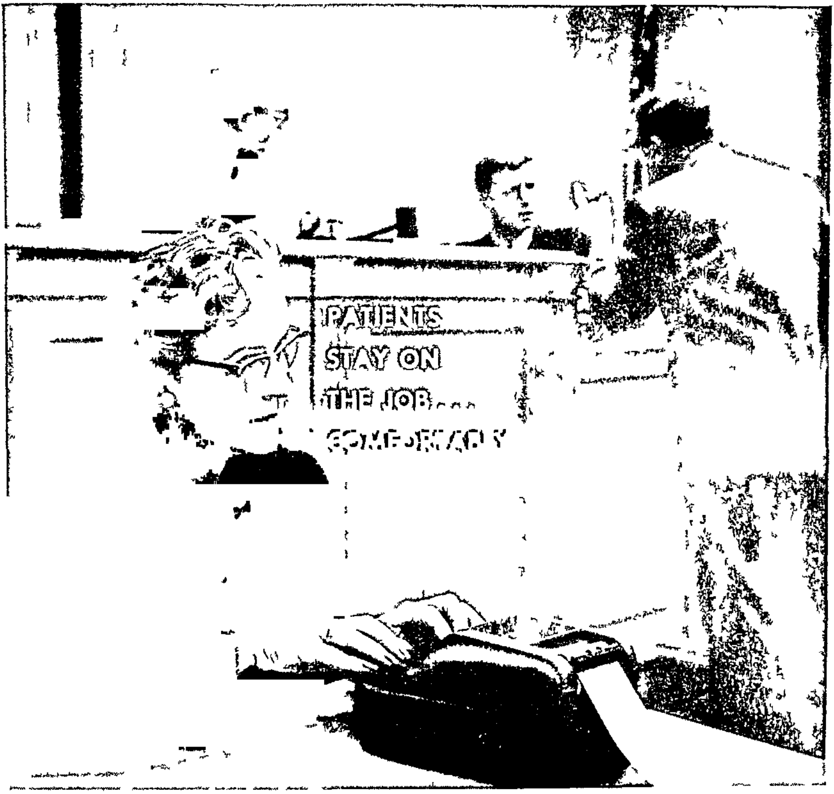

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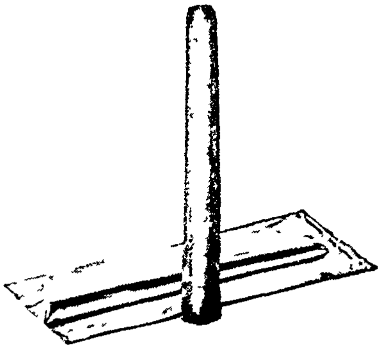

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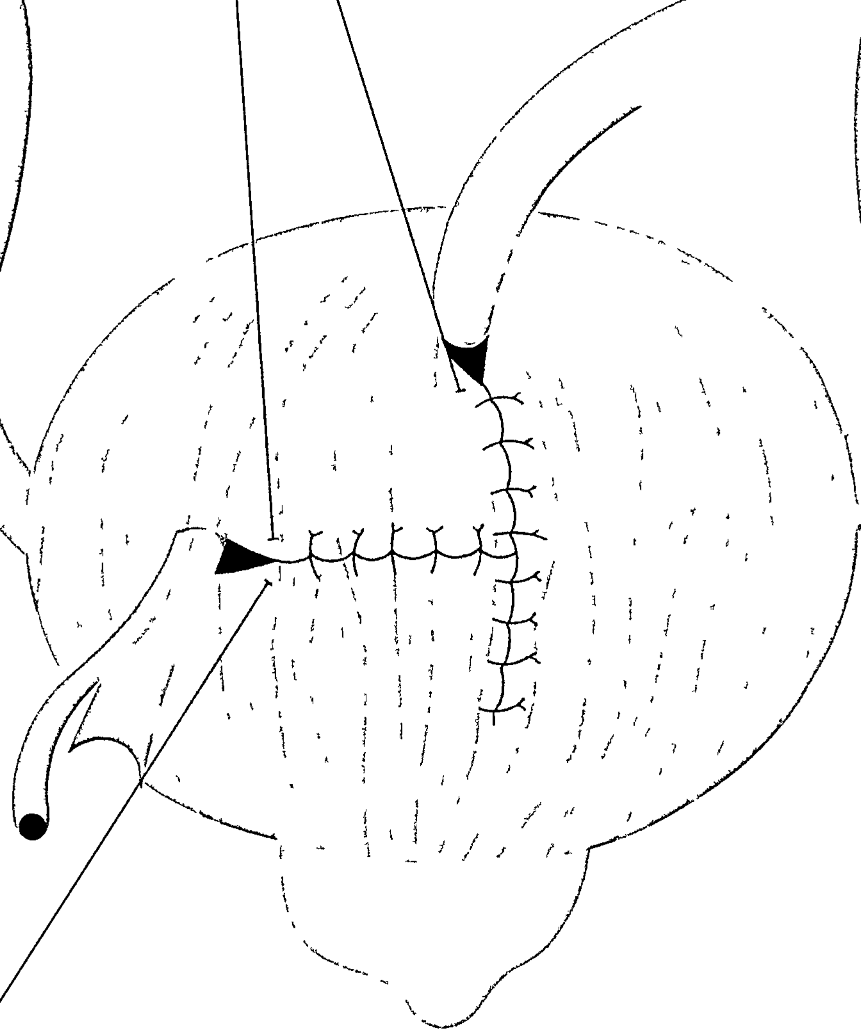

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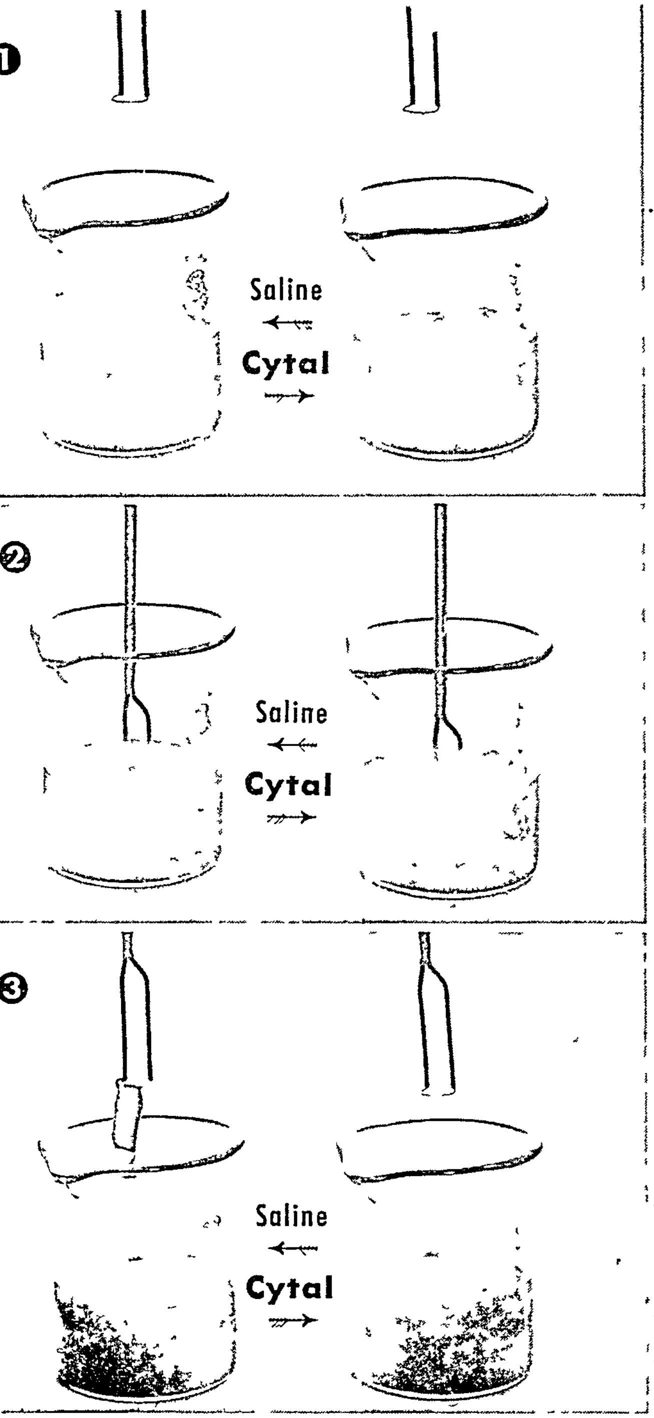

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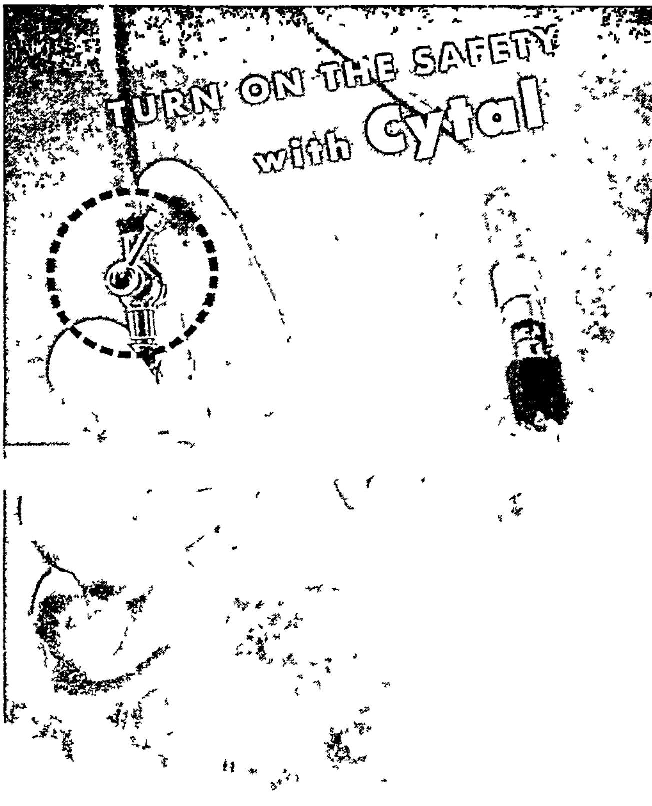

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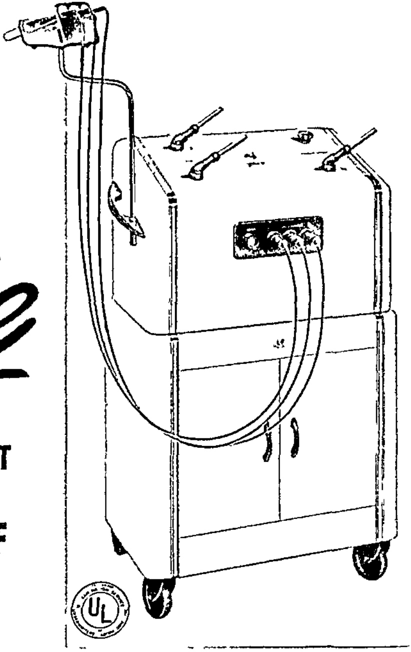

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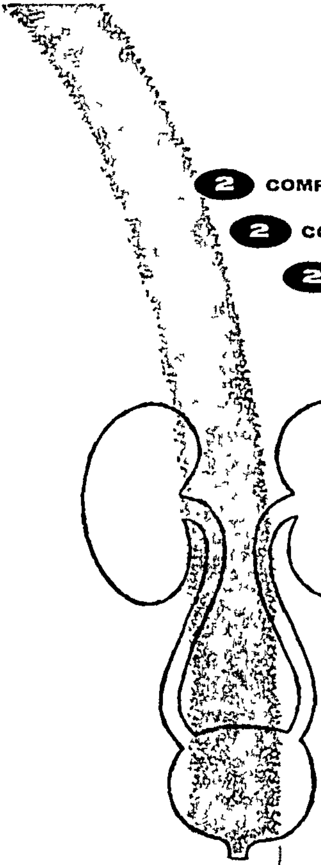

2 COMPONENTS

2 COMPLEMENTARY ACTIONS

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NOW . . both *pain* and *infection* are brought under quick, safe control *at their source* by the speedy, dual-action of the component drugs in—

*

RELIEVES LOCAL PAIN BY LOCAL ACTION

Phenylazo diamino pyridine HCl—enjoys a long clinical history as a local (not unwanted systemic) analgesic to the urogenital mucosa Relief from burning, pain frequency—in minutes in 90 per cent of cases.

REMOVES LOCAL INFECTION BY LOCAL ACTION

Sulfacetamide—sulfonamide of choice in urinary tract infections—unusually high solubility in acid urine so prevalent in pathological infections—hence (1) effective in 93 98 per cent of cases involving mixed organisms, and (2) safe—no kidney damage, no renal concretions no anuria

INDICATIONS

cystitis pyelitis urethritis (nonspecific) prostatitis pain and infection associated with kidney stones, urinary prophylaxis during pregnancy and gynecologic surgery

SUPPLIED

SULFID TABLETS - each coated tablet contains Phenylazo diamino pyridine HCl, 50 mg , Sulfacetamide, 250 mg Bottles of 100

SULFID SUSPENSION (Geriatric—Pediatric)—each teaspoonful (5 cc.) contains one-half the Sulfid tablet dosage

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BRAND OF NITROFURANTOIN

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Percentage of Effectiveness of Furadantin Against Various Strains of Bacteria in Vitro

	Aerobacter aerogenes	Proteus sp.	Paracolobactrum sp.	Micrococcus pyogenes	Streptococcus pyogenes	Escherichia coli	Pseudomonas aeruginosa
Furadantin	82.1	66.6	31.2	91.9	93.9	60.0	13.3
Antibiotic A	71.4	55.5	25.0	93.5	96.9	66.0	26.6
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Antibiotic B	3.5	0	0	66.1	63.6	0	2.2
Penicillin	3.5	0	0	27.4	39.3	0	0
Antibiotic C	14.2	7.4	18.7	46.7	72.6	22.0	11.1

ADAPTED FROM PERRY[2]

Furadantin's "high degree of effectiveness against bacteria responsible for urinary tract infections is brought out by this study."[2]

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SUPPLIED: Tablets, 50 and 100 mg., bottles of 25 and 100.
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REFERENCES: 1. Waisbren, B. A., and Crowley, W.: A.M.A. Arch. Int. M. 95:653, 1955. 2. Perry, R. E., Jr.: North Carolina M. J 16:567, 1955.

NITROFURANS—A NEW CLASS OF ANTIMICROBIALS—NEITHER ANTIBIOTICS NOR SULFAS

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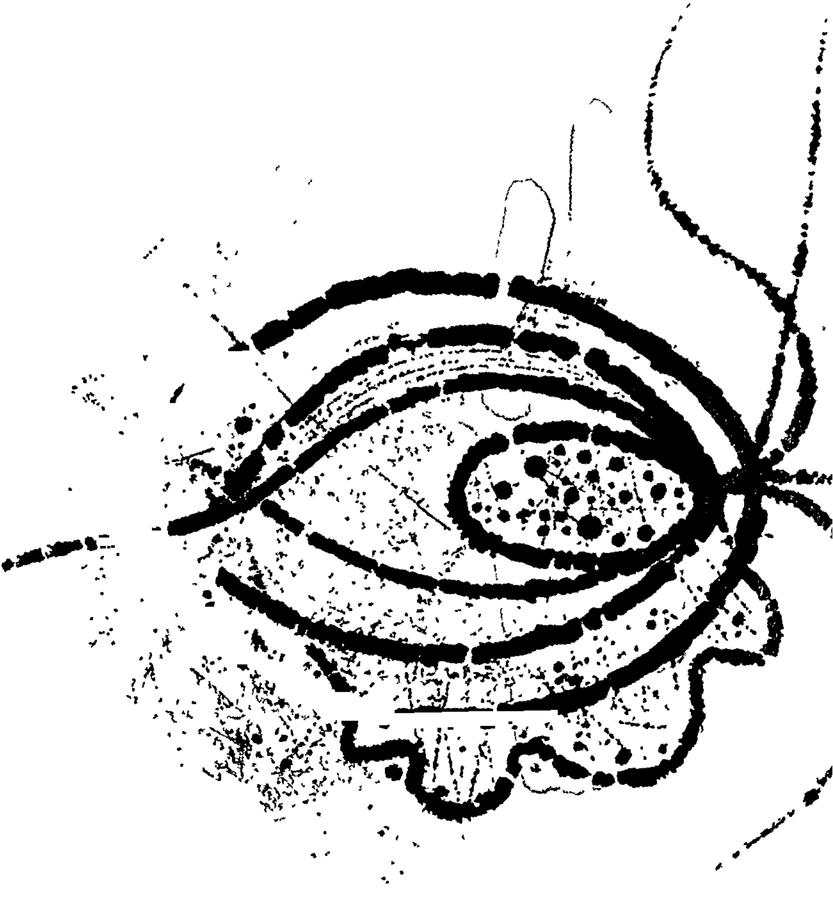


TRITHEON® TABLETS

brand of aminitrozole

...oral therapy

for trichomoniasis

in the male and female

1

TRICHOMONAS VAGINALIS INFECTION

prevalence of the disease

The protozoan flagellate *Trichomonas vaginalis* "...is now recognized as occurring in association with leukorrhea of vaginal origin more frequently than any one other specific organism...."[1] In approximately 25 to 35 per cent of women with symptoms of vaginitis, *T. vaginalis* is at fault.

Although vaginal trichomoniasis may be found in children and in women past the menopause, its greatest incidence is during the period of sexual maturity. It is somewhat more common in the nonpregnant state than during pregnancy, when candidiasis (moniliasis) occurs more frequently.

Approximately 58 per cent of males whose wives have trichomoniasis harbor the organism.[2] In a recent report, Coutts[3] notes that among 2,482 males with nongonococcal urethritis, *T. vaginalis* was found in 1,690 (68 per cent).

presenting complaints in women

"Leukorrhea is the most constant and the most characteristic symptom of vaginal trichomoniasis. Almost invariably, this is associated with some degree of irritation or itching of the genital structures, and, frequently, there may be other local complaints such as dysuria, dyspareunia, or irritation of the neighboring skin areas, particularly the inner aspects of the thighs."[1] Postmenstrual exacerbation of symptoms, particularly increased discharge and itching of the vulva, is common.[1]

clinical findings

vulva and neighboring structures—In the typical acute case, the labia are edematous and inflamed. There may be acute dermatitis of the perivulvar skin and the inner aspects of the thighs. The urethral orifice may be prominent or pouting and frequently contains the same discharge present in the vagina and on the vulva. Because of the general inflammatory reaction, associated involvement of Bartholin's or Skene's glands is difficult to detect.

vagina and cervix—The vaginal mucous membrane may be deeply congested and deep red or vermilion in color, instead of the normal pale pink. In some cases, the vaginal papillae are prominent and granular, so that the vagina assumes a "strawberry" appearance. The cervix itself is not involved. The external os and cervical canal are usually normal. However, in protracted and recurrent infection, endocervicitis and cervical erosion may develop.

discharge—Characteristically, the vaginal discharge has a pathognomonic "frothy" appearance. It is usually profuse, purulent, of a fluid consistency and often foul. Its color varies from creamy white to yellow-green to grayish yellow. In the presence of severe inflammation, the discharge may even be blood-tinged.

Fig 1.
Clinical appearance of the vulva showing "frothy" discharge characteristic of trichomoniasis

pathologic findings in the female

Trichomonas vaginalis is found in the exudate adjacent to the vaginal mucosa, in Bartholin's and Skene's glands and in other areas, along with leukocytes and a variety of secondary invaders. In trichomoniasis, the customary chief inhabitants of the healthy vagina, the Doderlein bacilli, either disappear completely or remain in markedly reduced numbers. The normal vaginal acidity (pH 4.0 to 4.8) decreases somewhat, so that the pH ranges from 5.0 to 6.0, with an average value of 5.5.

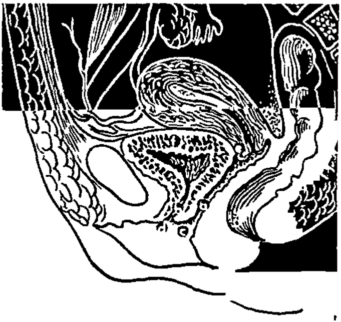


Fig. 2.
Hiding places of Trichomonas vaginalis in the female:

A. Vagina
B. Urethra
C. Bartholin's gland
D. Skene's gland
E. Endocervix
F. Bladder

infection in the male

In contrast to *T. vaginalis* infestation in the female, similar infestation in the male is often asymptomatic. For this reason, it has frequently been overlooked in the past. Infected husbands, even though asymptomatic, are a source of reinfection. The trichomonads may be present in the preputial sac, urethra, prostate, seminal vesicles, epididymis, bladder and, more rarely, the upper urinary tract.

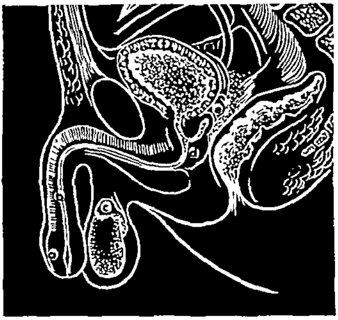


Fig. 3.
Hiding places of Trichomonas vaginalis in the male:

A. Preputial sac
B. Urethra
C. Epididymis
D. Prostate
E. Seminal vesicles
F. Bladder

2 DIAGNOSIS OF TRICHOMONAS VAGINITIS

clinical examination

The appearance of the vulva, the vagina and, particularly, the discharge is often so typical that the experienced observer can make the diagnosis of Trichomonas vaginitis by clinical inspection. However, not all cases of vaginal trichomoniasis present the customary appearance. Consequently, before starting treatment, it is advisable to verify the diagnosis by microscopic demonstration of the organism.

decisive diagnosis

wet smear—Although not as accurate as the culture method, the easiest, quickest and most convenient method of demonstrating trichomonads is by the wet smear. This requires only an ordinary glass slide.

For making a wet smear, a cotton-tipped applicator containing secretion from the posterior fornix is placed in 1 or 2 cc. of physiologic saline, Ringer's solution or Trichomonas Diluent, Ortho, rotated, removed and rolled on a glass slide. The smear thus made is then examined under low magnification. Trichomonas Diluent, Ortho, facilitates demonstration of trichomonads because with this diluent, trichomonads appear colorless and *motile*, while cellular components of the vaginal smear are pink and nonmotile. *T. vaginalis* is the only flagellated protozoan in the human vagina.

Under low magnification, trichomonads are readily detected as clear, actively motile, pear-shaped organisms, slightly larger than pus cells. Their body shape changes readily, and their movement is characteristically darting or jerky.

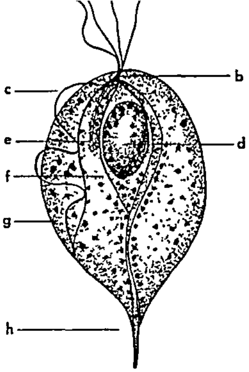
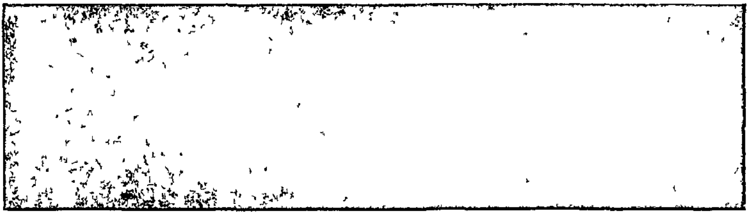


Fig. 4. Structure of Trichomonas vaginalis

A Four anterior flagella
B. Blepharoplast
C. Undulating membrane
D. Nucleus
E. Parabasal body
F. Parabasal fibril
G. Posterior flagellum
H. Axostyle



At the anterior end of *T. vaginalis* are four flagella which move with great rapidity. Along the side of the protozoan, starting from the base of the flagella and ending about midway along the body, is an *undulating membrane* which also beats rapidly. Extending from the posterior portion is a stiff appendage, the axostyle. Under continued observation, trichomonads can be seen to degenerate gradually. They become rounded ("pseudocyst"), disintegrate and ultimately disappear completely. There is no true cyst formation. Reproduction is by binary fission.

culture—Demonstration of trichomonads by culture is unnecessary in clinical practice. It is essential, however, in research projects and clinical investigations concerned with the efficacy of trichomonacidal agents. Only by negative culture can a distinction be made between *true cure* and apparent cure (*symptomatic relief*).

The recent work of Kean and Day[4] has substantiated the reliability of the culture method for detection of trichomonads. In 80 women with vaginal *trichomoniasis*, *culture with Simplified Trypticase Serum* (STS) *medium* was positive in 100 per cent. The hanging drop was positive in 76 per cent, and the stained smear in 74 per cent. In not a single instance was a patient positive by hanging drop or stained smear, and negative by culture.

3 NEED FOR SYSTEMIC THERAPY

cure versus temporary relief

Until the advent of systemic therapy with TRITHEON tablets, eradication of *T. vaginalis* had been difficult to obtain. Transitory symptomatic relief had been the usual result with all methods of topical treatment.

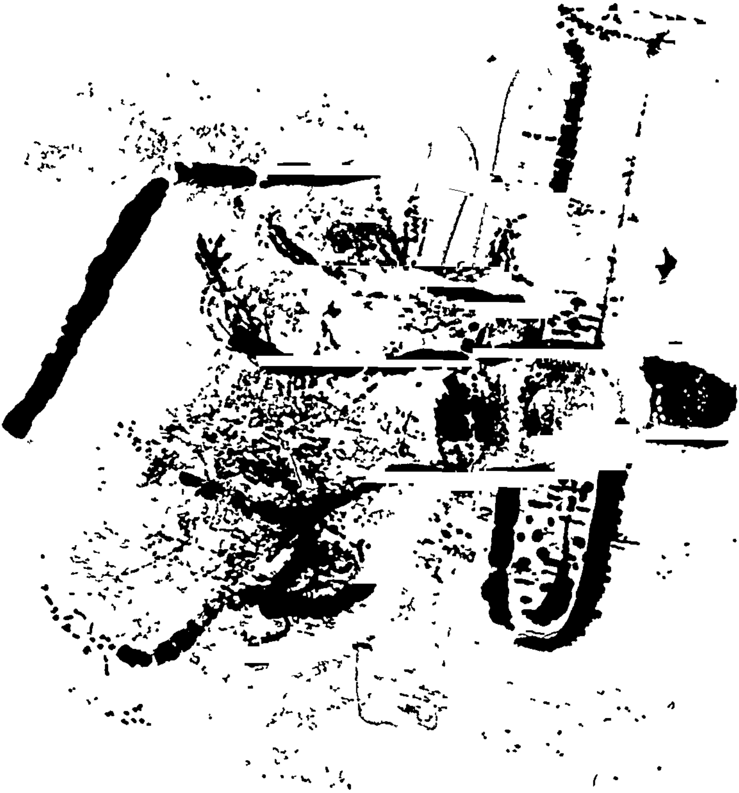
recurrences

There is a remarkable tendency to recurrence of Trichomonas vaginitis after apparent "cure." As noted by Trussell: "Failure to cure vaginal trichomoniasis is suggestive of resistant forms but also suggests that (1) rectal, urethral and glandular involvement were overlooked, (2) treatment has been inadequate or inappropriate, (3) reinfection has occurred, or that (4) a drug-resistant strain has developed."[5] *In the light of recent research, it appears that recurrences are due mainly to the inability of local therapy to eradicate the trichomonads from inaccessible places in the female urinary and genital tracts, and to reinfection from husbands.*

In view of the problems involved in trichomoniasis, it is evident that local therapy must often fail. Only systemic therapy, reaching all the hiding places of the trichomonads in both the female and the male, can possibly be expected to succeed in effecting a *true cure.*

criteria of cure

Symptomatic relief, though often readily obtainable, is not evidence of cure. From the practical clinical standpoint, negative smears indicate probable cure. In clinical investigations, however, conclusive evidence of cure of trichomoniasis can be established only by means of negative cultures. In all evaluations of TRITHEON tablets in males and females, proof of cure was established by culture methods using Simplified Trypticase Serum (STS) medium.[6]



4

CLINICAL EFFICACY AND SAFETY OF TRITHEON TABLETS

eradication of trichomonads

Clinical investigation has conclusively demonstrated that TRITHEON tablets administered orally eradicate trichomonads for culture-proved cure of more than 70 per cent of female patients whose husbands are treated simultaneously with TRITHEON tablets.[7]

case studies

In Perl, Guttmacher and Raggazoni's[2] series of 174 women whose husbands were not treated, 35 per cent were cured clinically and parasitologically. This was determined by *negative cultures* with STS medium done two weeks after cessation of therapy and repeated two to four weeks later. Similar results were obtained by Plentl,[8] who treated 78 patients, 30 of whom were pregnant.

In a series[2] of 48 males, the diagnosis of trichomonas infestation was established in 28, by culture of the seminal ejaculate. Of the 28 males treated with TRITHEON tablets, 16 were cured after one course of systemic treatment and two after a second course. The remaining 10 failed to bring in a post-treatment semen specimen.

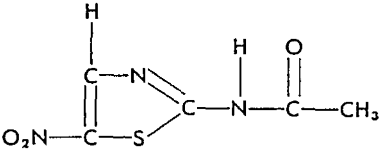
safety of TRITHEON tablets

TRITHEON tablets are well tolerated.[2,8] There has been practically no gastric intolerance, and side effects have been absent or negligible. No effect on the hemogram has been observed. In some patients the urine may be colored brown. This is due to a metabolite of aminitrozole and is not related to blood.[9]

5 ACTIVITY AND PHARMACOLOGY OF AMINITROZOLE

chemical structure

TRITHEON tablets are composed of 2-acetylamino-5-nitrothiazole (aminitrozole). They contain no arsenic, bismuth, silver, mercury, iodine or antibiotics and are completely different from other trichomonacides both in chemical structure and oral efficacy.



2-acetylamino-5-nitrothiazole (aminitrozole)

trichomonacidal activity in vitro

When compared with commonly used topical agents, the trichomonacidal effect of TRITHEON tablets is from 75 to 1,500 times as great.

comparative trichomonacidal efficacy

Agent	*Maximum Killing Dilutions (In Vitro)*
Aminitrozole (TRITHEON)	1:1,500,000
Phenylmercuric acetate	1:20,000
Silver picrate	1:18,000
5,7 diiodo-8-hydroxyquinoline	1:1,000
Bismuth glycolyl arsanilate	1:1,000

trichomonacidal activity in vivo

In vivo studies[9] utilizing the mouse peritoneum have also demonstrated the outstanding action of aminitrozole against trichomonal infection. White mice were inoculated intraperitoneally with pure cultures of *Trichomonas foetus* grown in STS medium. *T. foetus* was used rather than *T. vaginalis* because it is more pathogenic for the mouse. Aminitrozole was administered in varying doses, starting on the day of infection or on the fifth day after infection. Of the control animals, 95 per cent developed intraperitoneal infection and 55 per cent died. In the animals receiving aminitrozole, the morbidity and mortality rates varied from 0 to 10 per cent. The effectiveness was greater when the drug was administered early. The authors concluded that aminitrozole "...in dosages of 50 and 100 mg./kg. was highly or completely effective in eradicating the experimental body cavity infection of *T. foetus* in mice."[9]

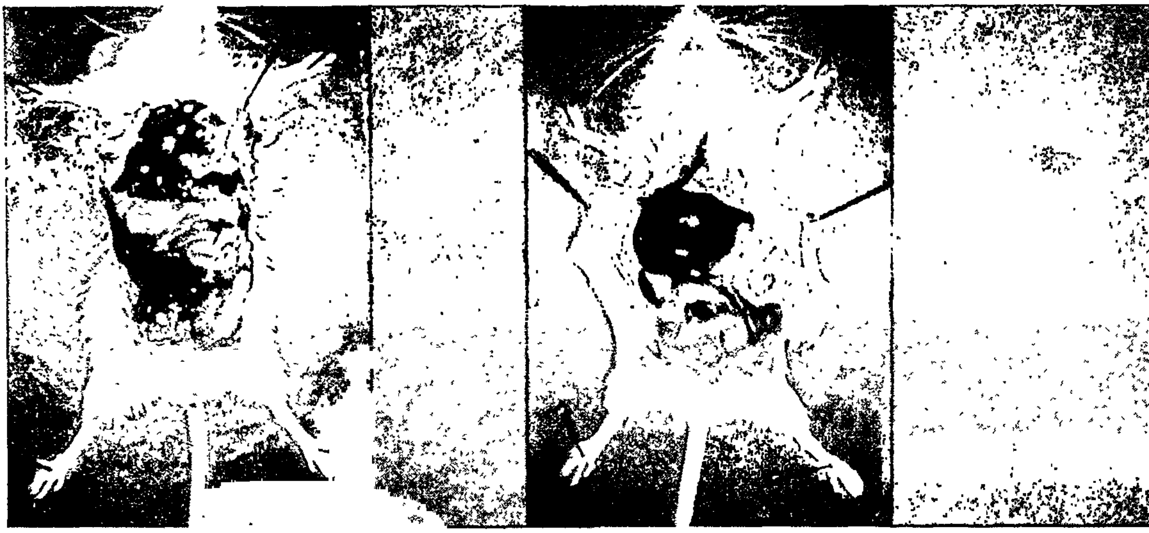


Fig. 5. Trichomonacidal action of aminitrozole:

A. Control: peritonitis following intraperitoneal infection with Trichomonas foetus.

B. Treated with 2-acetylamino-5-nitrothiazole: no peritonitis in similarly infected mouse.

results of toxicity studies

Exhaustive acute, subacute and chronic toxicity tests have established the safety of aminitrozole.[9] It is characterized by a low oral and intraperitoneal acute toxicity in several species (rat, mouse, chicken, turkey and dog). Subacute and chronic toxicity studies in the dog and monkey showed no evidence of impaired liver or kidney function, no change in the chemical constituents of the blood and no leukopenic effect.

6 TREATMENT WITH TRITHEON TABLETS

treatment in the female

Dosage is one tablet (100 mg.) orally, three times daily, for ten days. To speed relief of vaginal irritation and inflammation, adjunctive soothing local therapy may be prescribed. Aci-Jel® therapeutic vaginal jelly is particularly suitable because of its blandness and physiologic pH. In resistant cases, the course of treatment with TRITHEON tablets may be repeated.

treatment in the male

It is most important that the husband be treated at the same time as the wife. Dosage for the male is the same as for the female. To avoid reinfection, patients should refrain from marital relations during treatment.

TRITHEON TABLETS

brand of aminitrozole

indications:

TRITHEON tablets provide effective oral therapy for trichomoniasis in the male and female.

composition:

Each tablet contains 100 mg. of 2-acetylamino-5-nitrothiazole (aminitrozole).

recommended dosage:

One tablet orally, three times daily, for ten days. In resistant cases, a second course of treatment may be prescribed.

available:

Bottles of 30 and 180 tablets.

adjunctive therapy in the female:

To speed relief of vaginal irritation and inflammation, local therapy with Aci-Jel therapeutic vaginal jelly is recommended.

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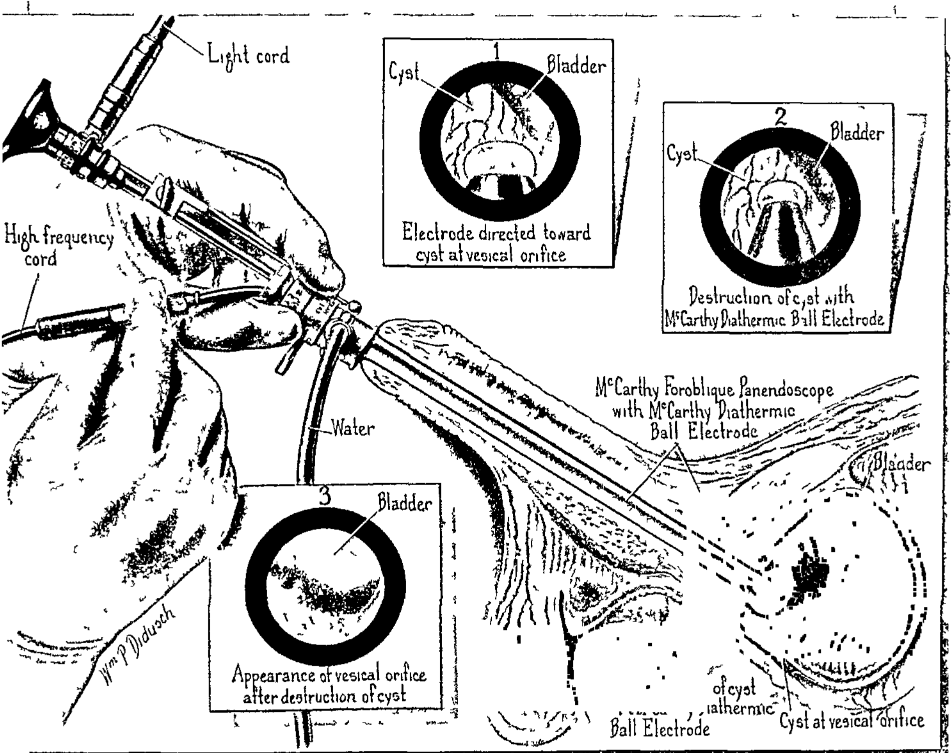
Mc Carthy
FOROBLIQUE PAN-ENDOSCOPE



Light cord
High frequency cord
Water
1
Cyst
Bladder
Electrode directed toward cyst at vesical orifice
2
Cyst
Bladder
Destruction of cyst with McCarthy Diathermic Ball Electrode
3
Bladder
Appearance of vesical orifice after destruction of cyst
McCarthy Foroblique Panendoscope with McCarthy Diathermic Ball Electrode
Bladder
of cyst
iathermic
Ball Electrode
Cyst at vesical orifice
Wm P Didusch

The illustration above shows the successive steps in the destruction of a cyst at the vesical orifice with the McCarthy Diathermic Ball Electrode passed through the McCarthy Foroblique Pan-endoscope, using a high frequency current.

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FREDERICK J WALLACE, *President*

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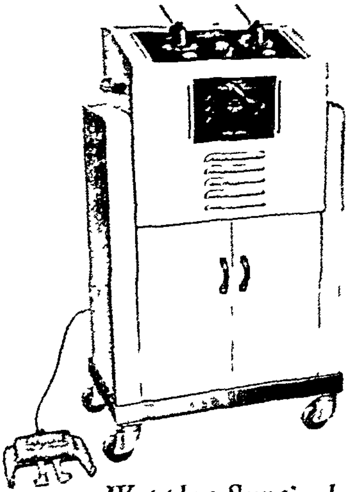

A.C.M.I. Electrosurgical Unit C-264

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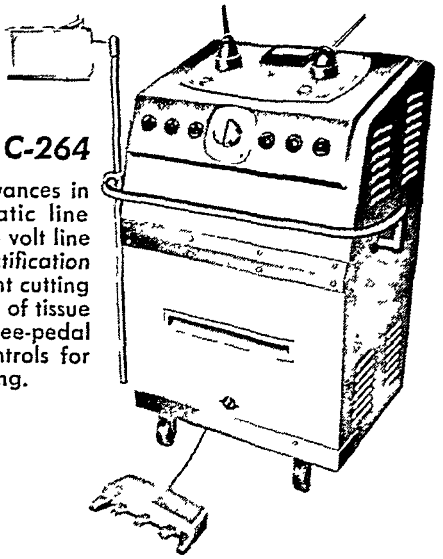

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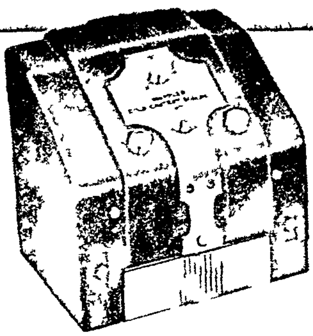

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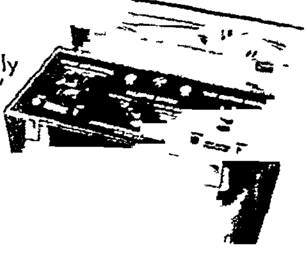

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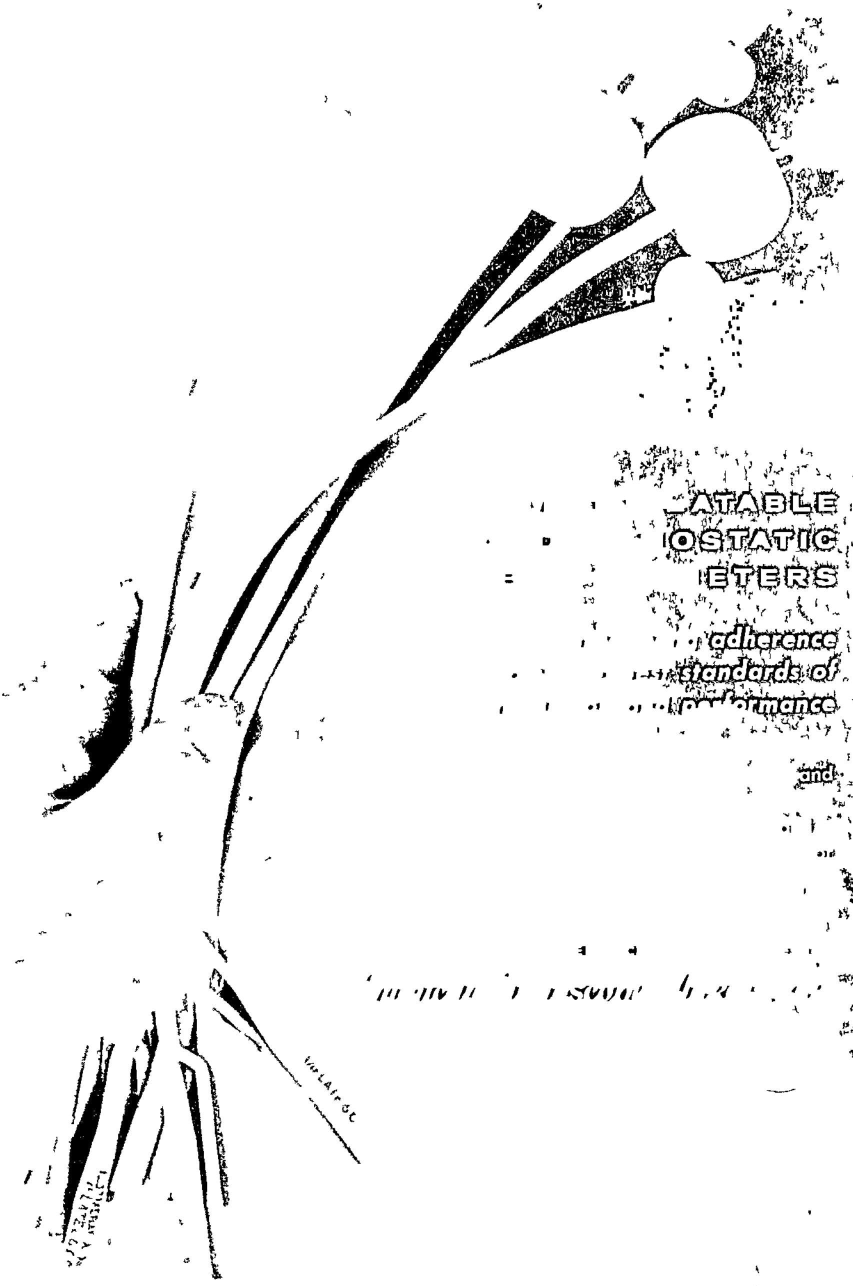

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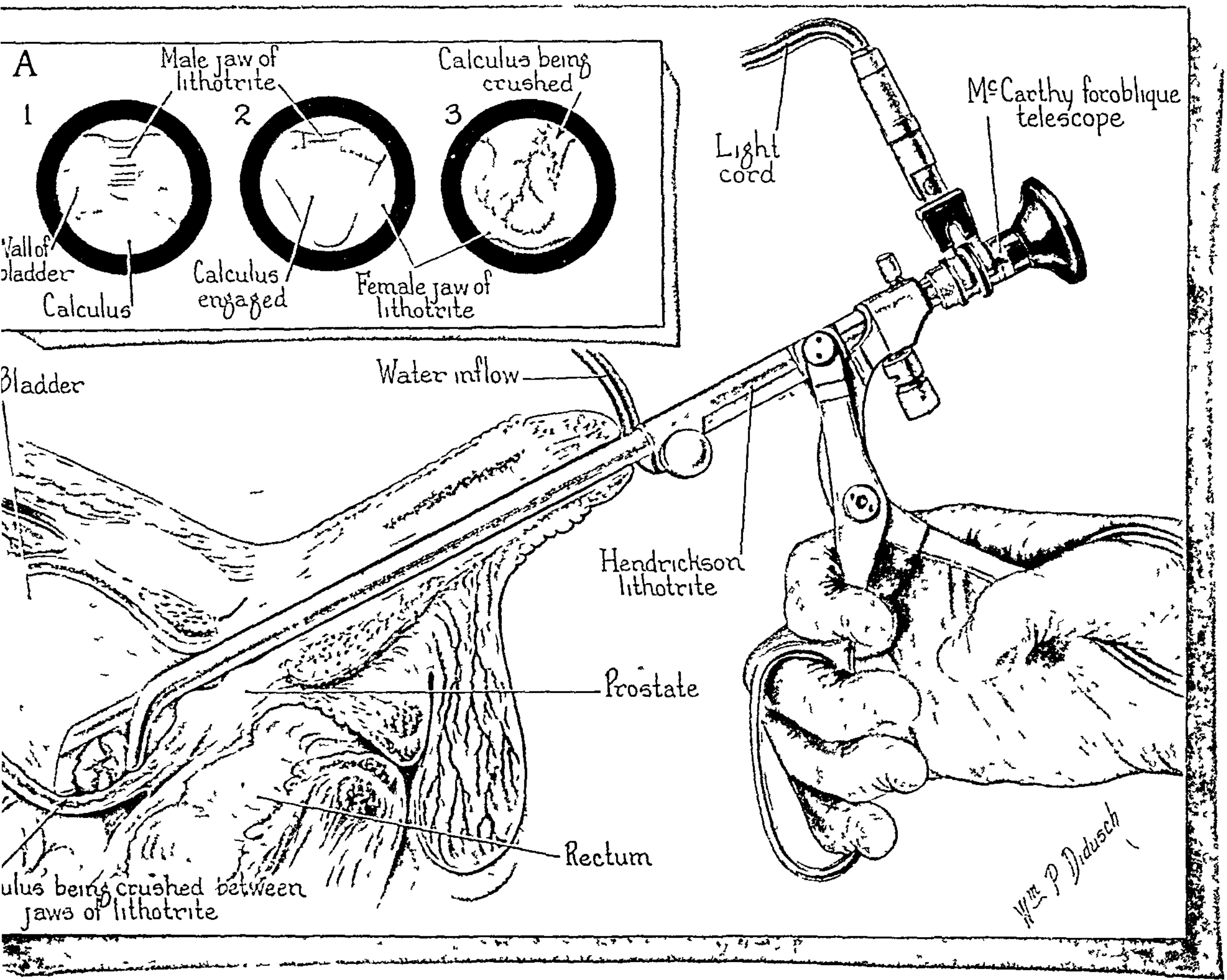
THE
HENDRICKSON LITHOTRITE

The Hendrickson lithotrite is believed the first ever made with a sliding type of jaw that has the lens and flow of water centrally located close to the field of operation. The angle formed between the jaws and the shaft of the instrument permits easy passage into the bladder. Size of shaft and jaws is 26F. The jaws are sufficiently strong so that it is unlikely that they can be broken by any but the most powerful man exerting force on the handles. The McCarthy foroblique 68A telescope affords excellent vision.



The illustration above shows a vesical calculus being crushed between the jaws of the Hendrickson lithotrite. Insert "A" consists of views as seen through the McCarthy foroblique telescope. 1. Shows the male jaw of the Hendrickson lithotrite behind the vesical calculus. 2. The female jaw has been pushed forward to engage the calculus. 3. Shows the calculus being crushed.

Catalog No. 4875 *See Your Dealer*

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The Journal of Urology
Vol. 75, No. 5, May 1956
Printed in U.S.A.

DIAGNOSIS OF INTERMITTENT HYDRONEPHROSIS: IMPORTANCE OF PYELOGRAPHY DURING EPISODES OF PAIN

REED M. NESBIT

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The urologist is often asked for an opinion in cases where the presenting symptom is pain in the upper abdominal quadrant, or in the kidney region. The causes of pain in these areas are many and most physicians, in all fields ranging from orthopedics to psychiatry, are beset with the problem of their differential diagnosis, for nerve root irritation, diverticulitis of the colon, or just ordinary fatigue can often produce symptoms identical to those of hydronephrosis, and the symptoms of hydronephrosis can be mimicked by Pott's disease, cholelithiasis, herpes zoster or other diseases. In seeking the cause of pain the attending physician often must call upon his colleagues in many fields when the diagnosis is obscure and in some instances a final diagnosis will depend upon the exclusion of various causes of pain. Yet this process of exclusion is manifestly a difficult problem when positive criteria are lacking.

The purpose of the present report is to point out the value of pyelography *during pain* in the urological study of such cases and to emphasize the important fact that patients who suffer from attacks of intermittent hydronephrosis may have pyelograms that are entirely normal between attacks. In such cases the urologist will miss the diagnosis completely if he assumes that normal pyelograms exclude the diagnosis of intermittent hydronephrosis, for such is not the case.

Persisting dilatation of the renal pelvis, of course, depends upon a continuing obstruction which interferes with normal emptying. And if the mechanism for causing intermittent hydronephrosis is a fascial band, or an aberrant vessel which might exert pressure upon the ureteropelvic junction only in unusual circumstances, then an abnormality of the pyelogram might occur only upon such occasions.

There are familiar examples of these transient phenomena. For example, pyelograms made during an episode of ureteral colic due to calculus will demonstrate either non-visualization or hydronephrosis, yet pyelograms made the day after the attack may be normal. And the studies of Stewart and of Bunge by means of delayed cystography have revealed the amazing fact that some children with ureteral reflux may have excretory urograms that are entirely normal, yet roentgenograms made during delayed cystography will reveal enormous dilatation of the ureters and renal pelves. Thus it is evident that the musculature of the upper urinary tract possesses great resiliency and that pyelograms which are normal do not necessarily exclude the possibility of intermittent obstructive uropathy.

A splendid example of the matter of our discussion was the first case that the

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Read at annual meeting, North Central Section of American Urological Association, Chicago, Ill., September 26–October 1, 1955.

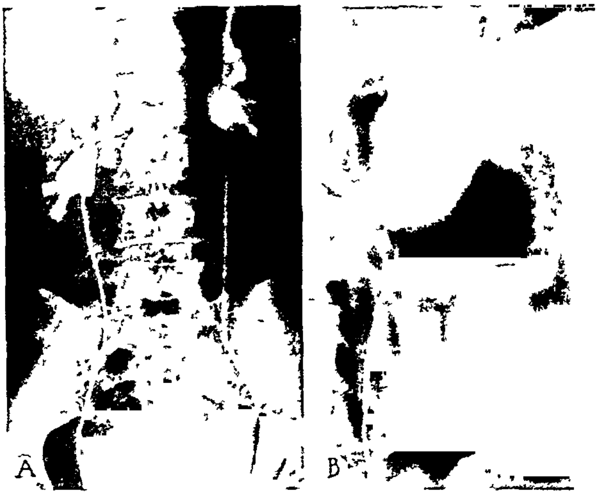

FIG. 1. Case 1. A, normal pyelograms made while patient was free from pain. *B*, hydronephrosis observed the following day during an attack.

present author encountered clinically. A 44-year-old woman was being studied in our hospital on the medical service for recurrent attacks of pain in the left upper abdomen accompanied by nausea and vomiting. All studies, including normal excretory urograms, failed to reveal the cause of her pain (fig. 1). While still in the hospital she had one of her attacks which our medical colleagues believed was typical of Dietl's crisis, and called upon us to see her again. Cystoscopy was performed during the attack and retrograde pyelograms were made which revealed the presence of a dilated renal pelvis not present the day before. Operation demonstrated an aberrant vessel which was the cause of the trouble.

Following this experience many years ago, it has been the practice on our service to advise repeat excretory urograms during an attack of pain in any patient suspected of having intermittent hydronephrosis whose original pyelograms are normal. To be sure, this policy has caused inconvenient delays in many instances, but it has resulted in establishing a diagnosis in many cases; and equally important, it has permitted us to exclude the diagnosis in many instances where normal pyelograms were made during typical attacks of pain.

A few illustrative cases will serve nicely to emphasize some points in question:

A 42-year-old man was referred because of repeated attacks of pain in the flank. His physician had put him through a complete investigation and concluded that his trouble must be due to ureteral obstruction. We made pyelograms which were normal and sent the man home requesting the doctor to make excretory pyelograms during an attack of pain. The man returned a short time later bringing with him a set of pyelograms which showed non-visualization on the side of his discomfort (fig. 2). He was free from pain on his arrival so we repeated the pyelograms which were now normal. Operation revealed an aberrant vessel, crossing the upper ureter, which was removed and the patient's difficulty was cured.

Another case is one of several that have been observed in which pain develops

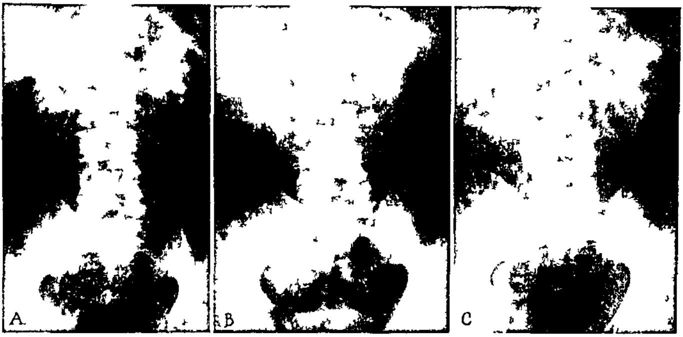

Fig 2 Case 2 *A* normal pyelograms made while patient was free from pain *B* non visualization of left kidney during attack *C* normal pyelograms following day when patient was comfortable

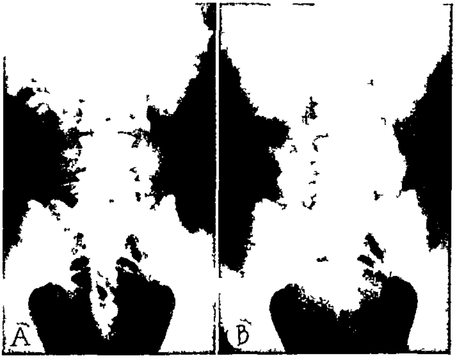

Fig 3 Case 3 *A* normal pyelograms made when patient was on normal fluid intake *B*, hydronephrosis with pain following ingestion of large amount of fluid

in the kidney following ingestion of large amounts of liquid A 22 year old man gave a history of having pain in the flank whenever he drank two bottles or more of beer When asked whether the same amount of any other beverage would produce the pain he remarked that he didn't know, having never tried it The ingestion of a large amount of water did reproduce the pain and pyelograms (fig 3) made before and during the attack revealed a significant enlargement of the pelvis when overloaded

Another case emphasizes the importance of reproducing the conditions of the attack in making the diagnosis A doctor's wife complained of pain in the kidney region whenever she lay on her back for more than a few minutes This pain was invariably relieved by a change in position, turning on either side or sitting up The pain never occurred when she was on her feet Excretory urograms had been made and these, although disclosing a duplication anomaly of the ureter, were otherwise normal. We had the patient lie on the x-ray table until she noticed pain and pyelograms made at that time revealed dilatation of both her renal pelves on that side (fig. 4); and when her pain was relieved by sitting, upright additional pyelograms showed that the dilatation had disappeared.

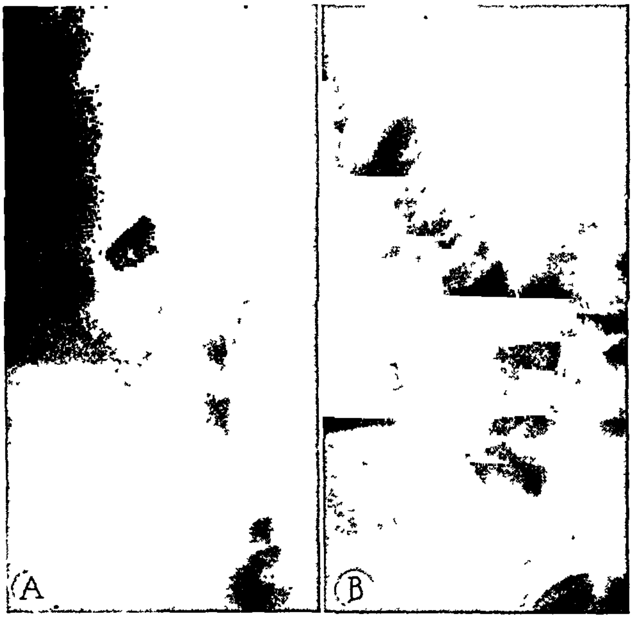

FIG. 4. Case 3. *A*, duplication anomaly of ureter. Pyelogram made with patient in upright position—and free from discomfort. *B*, dilation of both pelves resulted in renal pain. This occurred only when patient remained on her back.

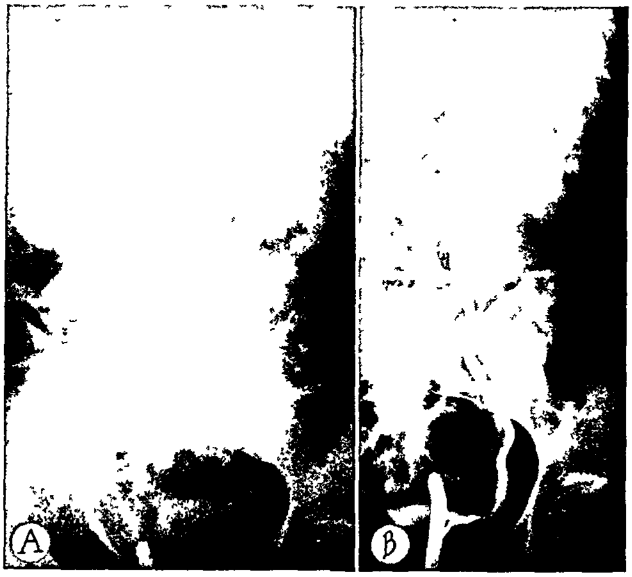

FIG. 5. Case 5. *A*, pyelogram made when patient was free from pain. *B*, pyelogram made during attack.

Nothing was done in the treatment of this case since knowledge of the innocuous cause of her pain sufficed.

The last case is one that was seen at Harper Hospital in Detroit and was presented at a pyelogram conference during a Detroit Branch Society meeting last year. We are indebted to Drs. Morley and Shumaker for permitting the use of this unusual case in the present report.

The patient had undergone extensive investigation for recurrent pain in the left flank. In spite of normal pyelograms her physician felt that she probably was suffering from attacks of Dietl's crisis and pyelograms were made during an attack (fig. 5). These demonstrated a massive dilatation of the renal pelvis. At operation an aberrant vessel was found to be the cause of the obstruction.

These then are examples of intermittent hydronephrosis in which the diagnosis depended upon pyelograms made while the patient was suffering from pain and point to the importance of this technique in pyelography. The diagnosis of hydronephrosis can sometimes be made only under these conditions and certainly cannot be excluded except in these circumstances.

The Journal of Urology
Vol. 75, No. 5, May 1956
Printed in U.S.A.

SOLITARY SEROUS CYSTS OF THE KIDNEY: BIOCHEMICAL, CYTOLOGIC AND HISTOLOGIC STUDIES

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The differential diagnosis of solitary serous cyst of the kidney from renal carcinoma usually requires surgical exploration. In a study of 85 proved cases of these two conditions, reported elsewhere (Clarke, Goade, Rudy and Rockwell), the authors concluded in agreement with other observers that there is no certain pyelographic or aortographic criterion by which a diagnosis of benign, serous cyst can be proved without operation. It appears, however, that there is a small group of patients who present a poor operative risk and in whom translumbar needle puncture of a cyst appears justifiable for diagnosis. This should be reserved for patients whose clinical findings and pyelograms strongly suggest cyst rather than tumor and in whom the mass can be shown, by nephrotomograms or aortograms, to be of spherical, avascular character.

Translumbar needle puncture permits radiographic study of the cyst after instillation of a small quantity of water-miscible contrast medium as suggested by Ainsworth and Vest. Before this is done, cyst fluid may be aspirated and studied for diagnostic purposes. In the present study are reported data from 18 proved solitary serous cysts of the kidney. It was our objective to determine whether or not the results of chemical, bacteriologic and cytologic examinations of the fluid were consistent enough to be of diagnostic value. In 11 patients, surgical excision of cysts was performed; one of these individuals (case 11) had two typical serous cysts of the left kidney. Translumbar needle puncture was carried out in the other six.

RESULTS

Fresh cell counts were done on the cyst fluid in 15 cases. No cells were found in 13, 2 lymphocytes/mm^3 in one specimen, 19 lymphocytes/mm^3 in one specimen. Papanicolaou preparations of the cyst fluid, done on 16 specimens, showed no malignant cells. The usual cytologic findings were flattened cells suggestive in appearance of desquamated serosal, squamous, or transitional epithelium.

Cultures of cyst fluid, made in 6 cases, were all negative.

In every patient, determinations of blood urea nitrogen and of serum protein, albumin, globulin, sodium, potassium and chloride were made and found normal.

Chemical analysis* of the clear, yellow cyst fluid in 18 cysts (table 1) indicated that it is a transudate of plasma. The urea, sodium, potassium, and chloride

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Accepted for publication January 11, 1956.

Aided by a grant from The Charlton Research Fund, Tufts University School of Medicine, Boston, Mass.

* Chemical analyses of cyst fluid and of serum were performed as follows: sodium and potassium with the Barclay flame photometer; urea nitrogen by the methods of Sobel, et al.; chloride by Van Slyke's method; proteins by the methods of Kingsley and of Wolfson, et al.

TABLE 1 *Chemical analysis of fluid from solitary cysts of kidney*

	Sex	Age	Side	Diameter, cm	Urea N, Mg %	Total Protein, Gm %	Albumin, Gm %	Globulin, Gm %	Sodium, Meq/L	Potassium, Meq/L	Chloride Meq /L
Operated Cases											
1	M	56	L	5	30	1.8	1.4	0.4	160	4.5	121
2	M	60	R	6	24	3.1	2.1	1.0	149	4.2	113
3	M	47	R	5	23	1.4	1.3	0.1	149	4.5	115
4	M	56	L	7	46	1.7	1.3	0.4	151	4.5	113
5	F	37	L	6	15	2.8			139	4.9	108
6	F	56	R	5	21	0.3	0.25	0.05	140	4.9	115
7	F	57	L	8	35	1.2	0.8	0.4	150	4.7	126
8	M	47	L	7	35	1.0	0.8	0.2	155	4.1	128
9	F	53	L	3	26	1.9	1.5	0.4	153	4.2	120
10	F	53	L	8	20	2.8	2.1	0.7	162	4.5	148
11	F	52	L	(Upper) 4	15	3.9	2.9	1.0	152	3.7	107
				(Lower) 4	17	4.4	4.2	0.2	145	3.5	103
Aspirated Cases											
12	F	48	R	8	42	1.6	1.2	0.4	142	4.2	131
13	F	69	L	6	16	0.8			141	3.8	108
14	M	61	L	25	27	3.0	1.7	1.3	152	4.2	114
15	F	56	L	10	27	3.2	1.8	1.4	141	3.5	117
16	M	67	L	7	33	0.8	0.6	0.2	145	4.4	110
17	M	67	R	7	19	4.2	3.0	1.2	141	4.1	107
Average		56			26	2.2	1.7	0.6	148	4.2	112
Upper limit of normal for serum					20	8	4.5	3.5	143	5	105
Lower limit of normal for serum					10	6	3.5	2.5	137	4	97
Hydrocele											
A					22	0.5	0.4	0.1	141	5.0	138
B					17	3.3	2.6	0.7	140	3.8	106

TABLE 2 *Histology of excised solitary kidney cysts, 21 cases*

Type of cells lining cyst	
Flat	18
Indistinct	3
Elements in cyst wall	
Collagenous tissue	21
Smooth muscle	1
Glomeruli	5
Tubules	17
Lymphocytes or monocytes	17

levels were within or a little above the normal serum range. Albumin content was reduced in each instance, globulin greatly reduced.

To aid in the interpretation of these findings, histologic sections from the walls of 21 typical solitary, serous cysts were studied (table 2). Nine of these cases were patients whose data appear in table 1; the other 12 represented the remainder of cases in our hospital files from which satisfactory histologic material could be obtained.

DISCUSSION

Our data indicate that the cellular lining of solitary renal cysts in section resembles mesothelium or endothelium. Desquamated elements, examined in Papanicolaou preparations, have a morphology consistent with origin from this type of tissue. Biochemical studies of the fluid indicate that it is a transudate of plasma. These findings proved consistent enough in our study to warrant their use as diagnostic criteria in the few cases of renal solitary cyst in which translumbar needle puncture rather than surgical exploration appears to be the method of choice in diagnosis and treatment.

The data, though of interest, are not of clear significance in interpreting the pathogenesis of solitary renal cyst. Some of these lesions may be of congenital origin, as indicated by their occasional appearance in patients as young as 16 months (Albarran and Imbert, cited by Kretschmer). In Hepler's review, he has presented evidence that the lesion may develop rather rapidly during adult life. He reproduced the lesion experimentally in rabbits by obstructing the papillae and interrupting the local blood supply. The condition is well recognized as occurring most commonly among patients at ages when arteriosclerotic or other vascular degenerative lesions are usual. An ischemic hypothesis on etiology is an attractive one.

The relationship of solitary, serous cysts of the kidney to polycystic disease is not clear. The latter condition has congenital and familial aspects (Simon and Thompson). Bagg found the lesion in the offspring of experimentally irradiated mice. Polycystic disease sometimes appears with other anomalies such as cystic lungs, liver, or pancreas; or with meningocele or polydactylism (Norris and Herman). Kampmeier showed that cystic tubules occur frequently in embryos and that polycystic disease may represent their nondisappearance in later life.

Embryonic nonunion of developing nephrons with tubular collecting systems has commonly been proposed as a factor in the pathogenesis of polycystic disease. Lambert's micro-reconstruction studies indicate that in the adult at least many of the cystic elements have continuity with the collecting system though in newborn polycystic kidneys the cysts are closed units. By inulin injection studies he showed persistence of glomerular function within cystic nephrons.

Bricker and Patton in a study of 6 cases of polycystic disease and four of simple cysts, found that inulin and PAH injected intravenously appeared in significant concentrations in fluid of polycystic disease but not in the solitary cysts. The sodium, potassium, and chloride values of polycystic cyst fluid approximated and usually slightly exceeded the normal plasma range. Sodium, potassium, and chloride also appeared in the fluid from solitary cysts in quantities within or slightly above the normal plasma range Protein content was low in polycystic and simple cysts alike The data of Bricker and Patton suggest that in polycystic disease the cysts are functionally connected with nephrons There is no evidence from their study or from ours that this is the case in solitary serous cysts

SUMMARY

The fluid from 17 cases of simple cysts of the kidney was analyzed and found to be a transudate of plasma Urea, sodium, potassium, and chloride levels were within or slightly above the normal plasma range Albumin content was reduced and globulin content was greatly reduced below normal values for plasma

Microscopic study of the walls of 21 solitary kidney cysts showed them to consist of fibrous tissue lined with flattened epithelium resembling endothelium or mesothelium Usually, degenerated nephrons, chronic inflammatory cells, and occasionally smooth muscle, were found imbedded in the collagenous tissue of the cyst walls It is reasonable to conclude from these observations that solitary cysts of the kidney are of serous character, although the mechanism of their formation remains incompletely explained

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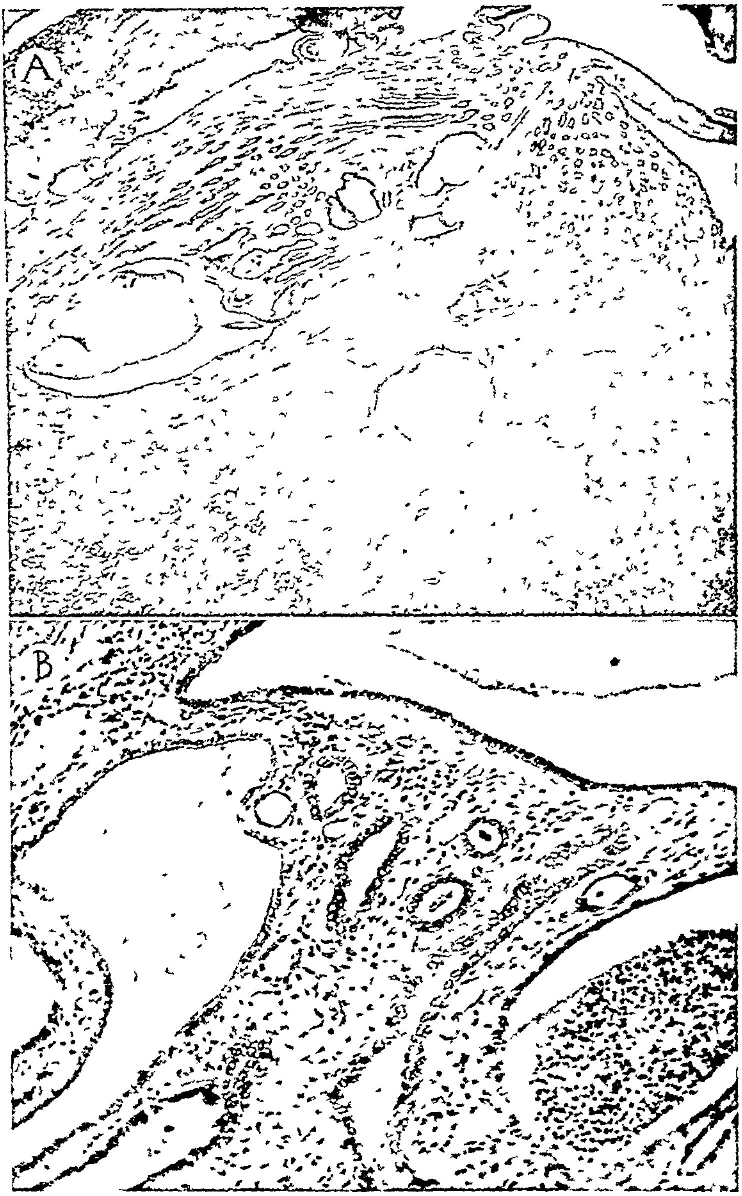

Fig. 3

cysts. Clinically there was insidious anemia and uremia. The cysts were mostly in the pyramids but scattered in the cortices. These cases differ from the one reported here by being contracted rather than enlarged.

Several articles have been published in the Journal d'Urologie on "Cystic Disease of the Renal Pyramids or Spongy Kidney." This journal has not been available to us for review.

Any attempt to explain the genesis of the cyst in this case invokes a consideration of polycystic kidneys. McKenna and Kampmeier's explanation[4]

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[4] McKenna, C M. and Kampmeier, O. F.: J Urol., 32: 37–43, 1934.

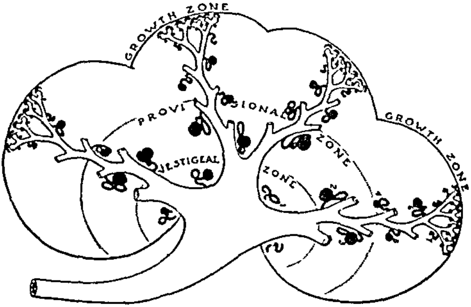

Fig 4. Vestigial zone, provisional zone, growth zone From McKenna and Kampmeier, J. Urol., 32: 37–43, 1934

involves the generations of collecting tubules successively branching from the ureteral bud Ordinarily these invest in vesicular masses in metanephrogenic mesoderm forming the uriniferous tubules The first generation of tubules developing with the first budding of collecting ducts is vestigial, the tubules having no glomeruli, and rarely joining the primary collecting ducts These usually disappear without a trace The next several generations have glomeruli and unite with collecting ducts After a short time the ducts are detached and some grow to cystic proportions and then disappear Persistence may result in solitary cyst This has been designated the "provisional zone" (fig 4) The outermost "growth zone" is the definitive cortex The writers believe that if cystic tubules cause sufficient pressure on adjacent normal tubules, normal union and development are prevented (fig 4)

Persistence and cystic dilatation of uriniferous tubules in the "provisional zone" afford a possible explanation for the cysts in our case

In 1947, Lambert[5] found in serial sections and reconstructions of polycystic kidneys, three types of cysts in the adult group One of these is designated as the excretory cyst of the medulla These were formed from collecting tubules and usually continued as undilated ducts of Bellini into the calyx Rarely the cyst was at the distal portion of the collecting duct and opened directly into the calyx Lambert believed that failure of union of nephrons with collecting tubules, incomplete growth of the tubule of the nephron and constriction of collecting tubules by fibrous tissue were excluded as causes for polycystic kidneys

We are not prepared to state whether the cysts in our case arose from persistent uriniferous tubules of the "provisional zone" or from collecting tubules as excretory cysts of the medulla in adult polycystic disease Perhaps there is an acquired tubular obstruction causing dilatation

We believe that the disease constitutes a distinct but rare clinical entity and that the term "cystic disease of the renal pyramids" is most appropriate

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
Printed in U.S.A.

RENAL VEIN THROMBOSIS

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Hemorrhagic infarction of the kidney due to thrombosis of the renal vein is a relatively uncommon condition and clinically is generally overlooked. The incidence of only 4 cases among 1,092 autopsies done at the Childrens' Memorial Hospital in Montreal, over a 12-year period[1] represents 0.37 per cent. Most figures place the incidence at lower than 1 per cent. The disease occurs more frequently in children than in adults and the diagnosis is seldom made preoperatively. We wish to report our case to show the difficulty of diagnosis and to emphasize the importance of a complete urological study.

The excellent review of the literature by Regan and Crabtree in 1948[2] of 90 cases of renal infarction of all types, with a report of 4 cases of their own in adults is recommended to the reader: "Venous infarction is a much more serious disease than the aseptic arterial infarction. Of the 20 cases of venous infarction reviewed, eight died. The condition was unilateral in sixteen, twelve of which had nephrectomy and survived. Four bilateral cases and four unilateral patients died." A brief review of the pathology of this condition is presented.

PATHOLOGY

Renal infarcts are of three types, a) ischemic, b) hemorrhagic and c) combined. Arterial and functional infarcts are ischemic, while venous infarcts are hemorrhagic. In some instances, combined infarcts are caused by simultaneous arterial and venous thrombosis.

According to Arthur C. Allen,[3] "thrombosis of the renal vein is generally although not always different in adults and in children. In infants, particularly in the newborn, thrombosis of the main renal vein is associated with massive hemorrhagic infarction of the kidneys. It is observed in infants, especially those with severe diarrheal diseases and dehydration. Previously considered rare, total hemorrhagic renal infarction was observed in 4 of 25 autopsy cases of Barenburg et al.[4] In two of them, infarction was accompanied by thrombosis of the main renal vein. The thrombus was usually confined to the main renal vein." In six of the 8 cases of hemorrhagic infarction of the kidney collected from the literature by Regan and Crabtree,[2] the patients were infants and there was thrombosis of the main renal vein in each. The associated diseases of these infants were: gastroenteritis in 4, lobular pneumonia in 1, and cellulitis extending from an abscess

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Read at annual meeting of Northeastern Section of American Urological Association, Lake Placid, N. Y., September 22-24, 1955.

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in the groin in 1 The ages of the patients (5 male, 1 female) were 9 days, 13 days, 2 months, 3 months and 3 years Three of the infants survived nephrectomy The other 2 cases were in adults, 20 years and 33 years of age, in whom the infarction developed 5 days and 65 days postpartum

Allen further states, "bilateral total hemorrhagic infarction of the kidneys is invariably fatal Patients with unilateral massive hemorrhagic infarction occasionally may be salvaged by prompt nephrectomy" He wrote, concerning the pathologic physiology, that "cases of hemorrhagic infarction occurring without thrombosis of the renal vein raise the possibility that when thrombosis is present it is secondary to the infarction However, it is in most cases nevertheless true that the venous thrombosis caused the infarctions In those instances where the thrombosis extended into the renal veins from the inferior vena cava no other interpretation seems likely In adults thrombosis of the renal vein produces generally a clinical picture of the nephrotic syndrome This syndrome appears to be on the basis mainly of a loss of protein, especially albumin in the urine as a consequence of abnormal glomerular permeability transmitted from the increased venous pressure"

Histologically there may be only relatively mild changes in the renal parenchyma The kidney structure shows hyperemia and hemorrhagic areas There is some tubular atrophy and interstitial edema with fibrosis The glomerular capillaries may show thrombosis or may be bloodless The tubular epithelium may show a mild degree of degeneration due to compression of them by the hemorrhage in the interstitial tissues Liquefaction may occur in fossae, forming abscess like cavities in which no bacteria can be demonstrated Cultures from the kidney are usually negative

CASE REPORT

P L, a 72-year-old man, was admitted to the medical service of Clifton Springs Sanitarium and Clinic, Clifton Springs, New York on May 1, 1954, with a chief complaint of recurrent pain in the left flank and left back His illness began on the night of April 28, 1954, when there was a gradual onset of pain which seemed to begin first in the left lower quadrant, gradually shifting around to the left flank and then into the left lumbar region The pain was described as steady and was aggravated by motion of the trunk and he found it difficult to get into a comfortable position The pain was not aggravated by coughing or deep breathing The following night the patient had very severe pain in the left lumbar region, for which his family physician gave several doses of pantopon before relief was obtained Most of the pain seemed to be in the left side of the abdomen The following morning the pain recurred Some of it was in the left upper quadrant, but mainly it seemed to be around toward the back and the left flank There had been no nausea or vomiting, no chill and no burning or frequency of urination, but an elevation of temperature was present Prior to admission an x-ray of the lumbar spine was said to show hypertrophic changes of L-1, L-2 and L-3 The patient also had 2 blood counts and 2 urinalyses, all said to have been normal He was finally admitted to the hospital on the medical service for further study

The past history revealed that he had been a patient in this clinic in May 1946, for a severe upper respiratory infection. Consultation at that time with the cardiologist revealed generalized and cerebral arteriosclerosis. An electrocardiogram was normal. In January 1951, he had a severe coronary occlusion following which he retired. He got along fairly well except for dyspnea and recurrent pains in the lower legs and arms upon exertion and on walking too far and too fast. Momentary rest would relieve both the arm and leg pains. He had a second coronary occlusion in February 1954, and was taking things easy when the present illness began. He never had any ankle edema and he never used nitroglycerine. His appetite had always been good and only rarely had there been indigestion. There was no history of jaundice and tarry or clay colored stools. He had nocturia 1 to 2 times, occasional hesitation, and never had any dysuria or complete retention. He had not been taking any continuous medication regularly until the present illness began.

On physical examination his temperature was 100.4F, pulse 104, respirations 22. He did not appear acutely ill but he was slightly confused regarding recent events. His heart had a regular rhythm. Sounds were of fair quality. There was a soft systolic murmur at the apex and the blood pressure was 115/70. His chest showed some dullness and somewhat diminished breath sounds at the left lower lateral lung field posteriorly. Pressure over the lower left lateral rib margin revealed slight pain. There was pain on the left side upon motion of the thorax. The abdomen was slightly distended, and quite tympanitic throughout. There was slight pain to fist percussion in the left flank and slight tenderness over the course of the descending colon. No masses were present and the liver, spleen and kidneys were not enlarged. The prostate showed minimal hypertrophy and was slightly nodular. The rest of the physical examination was essentially negative. Electrocardiogram on admission showed an old anterior and posterior infarction.

Laboratory studies on admission revealed an erythrocyte count of 4,060,000 per cubic mm.; hemoglobin 13.0 gm., 83 per cent. The leukocyte count was 9,500 with a differential count of polymorphonuclear leukocytes 69 per cent and 31 per cent lymphocytes, platelets plentiful. The urinalysis showed a slight trace of albumin, sugar negative; microscopic, a few red blood cells, occasional white blood cell, few coarsely granular casts and 2 to 3 finely granular casts seen. Wassermann was negative. Sedimentation rate was 38 mm. per hour, corrected. The fasting blood sugar was 106 mg. per cent and the urea nitrogen was 31.6 mg. per cent.

On fluoroscopy a definite hiatus hernia of the gastroesophageal type was demonstrated with marked redundancy to the esophagus itself and a posterior displacement of the normal course. Upper gastrointestinal x-ray series showed approximately one-third of the stomach permanently above the diaphragm, and there was a radiolucent area lateral and anterior to the herniated fundus, which on fluoroscopy appeared to represent the splenic flexure. The rest of the stomach and duodenum appeared normal. At 24 hours the barium had reached the splenic flexure but did not progress any further. X-rays of the abdomen the following day still showed the colon to be below the diaphragm.

Following the barium study the patient was temporarily free of pain and it was thought that perhaps the reduction of the colonic herniation was responsible for the relief of pain. However, the pain in the left flank recurred that same night. It was, therefore, thought that this was not the answer to the man's trouble and a further search had to be carried out. Meanwhile his cardiac condition remained the same, the blood pressure was 120/75, and there was no evidence of congestive failure. He had no chest pain nor dyspnea and no nausea or vomiting. He continued to run a low grade fever, below 100F, and continued to have more pain in the left upper abdomen and left flank. His abdomen was somewhat distended and he appeared more ill than on admission. A repeat blood count 5 days after admission showed an increase in his leukocytes from 9,500 to 10,900 and an increase in neutrophiles from 69 per cent to 77 per cent. Seven days after admission, the patient still complained of marked pain in the same region and his fever continued. However, for the first time hematuria was noted, 8 days after onset of pain. Another urinalysis showed gross blood. Blood urea nitrogen on the same date was 23.7 mg. per cent and serum chlorides 104 mEq/L. Stool examination showed benzidine reaction two plus and guaiac reaction negative.

On May 10, 1954, excretory urography showed a dilatation of the left ureter throughout the entire study and poor concentration of the dye bilaterally (fig. 1, *A*). This was thought to represent a possible obstruction of the left ureter.

The patient was accordingly referred to the urological department. Cystoscopy revealed the bladder to contain 150 cc of cocoa-colored bloody residual urine. A minimal degree of prostatic hypertrophy involved the lateral and median lobes. Marked choking of the left ureteral orifice and the intravesical portion of

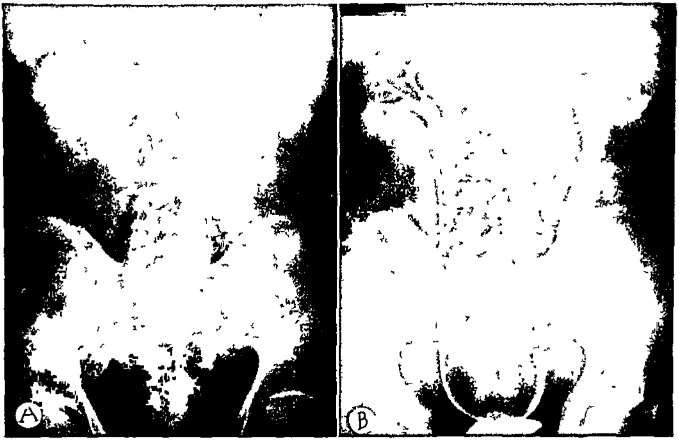

FIG 1. *A*, 20 minute excretory urogram showing poor dye excretion of both kidneys, dilatation of left ureter and pelvis and bizarre appearance to left pelvis. *B*, retrograde pyelogram showing dilation and bizarre appearance of left kidney pelvis with filling defect due to blood clots

the left ureter was noted. Cloudy, bloody urine was seen extruding from this orifice. The right orifice was normal in appearance and was draining clear urine. The rest of the bladder appeared normal, there being no evidence of tumor, stone, ulcer or diverticulum, and the bladder held 500 cc. Catheters were readily advanced up both ureters, there being no obstruction encountered on either side. The drainage of urine from the right kidney was clear, while that from the left kidney had the same appearance as that in the bladder, i.e., cocoa colored, indicating that the blood was coming from the left kidney. Cultures from the bladder and the right and left kidneys were all negative. Intravenous indigo carmine appeared in a fairly normal concentration within 6 minutes from the right kidney, but there was no evidence of the dye coming from the left. Retrograde pyelograms showed a characteristic picture suggesting advanced tumor involving the greater portion of the left kidney (fig. 1, *B*). It appeared as if the tumor was arising from the calyces of the middle infundibulum. Metastatic x-ray survey was negative. The patient was prepared for left nephrectomy with a tentative diagnosis of tumor of the left kidney. At operation on May 17, 1954, a great deal of inflammatory reaction of the perirenal fat was found, which was quite adherent, hard and friable. The left kidney was larger than normal and was dark red in color and mottled. The hilar fat also showed a hyperemic inflammatory reaction. The capsule was tense and hemorrhagic, as well as the parenchyma throughout. Nephrectomy was done. Postoperative course was excellent and the patient was discharged on the eleventh postoperative day, May 28, 1954. He was seen in the office several times and finally discharged on August 4, 1954, feeling and looking well. He was also seen by the internist who first attended him. His blood pressure was 130/85 and upon fluoroscopy the heart was slightly enlarged but there was no evidence of the original air-containing organ in the left chest. Apparently the intrathoracic hernia had reduced itself.

The patient is still alive and well and enjoying good health. The remaining kidney is functioning normally and the urine is clear.

The pathological examination showed grossly a kidney of normal shape and somewhat large. The fat near the kidney was of increased firmness, hyperemic and resembled that of perinephritis. The kidney measured 12 by 6 by 6 cm., and the capsule stripped easily. The exposed cortical surfaces were irregularly mottled with hemorrhagic and pale areas. The cut surfaces showed some atrophy of kidney substance. Small arteries of cut surfaces were thickened and gaping. The attached ureter was not much dilated but the pelvis and calyces were dilated and filled with blood clots. The mucosa throughout was granular and yellowish. The bleeding into the drainage system was quite massive and some of the clots appeared fairly old. Careful search for tumor was made but none found. There were round to oval circumscribed areas of blood clot in the hilar fat, which showed organization and appeared to be intravascular. The main renal vein was occluded by an old thrombus and was dilated. Microscopic examination showed areas of cortical scarring and a marked degree of arteriosclerosis of the branches of the renal artery. The renal artery showed no evidence of thrombosis or occlusion. In several sections there was old organizing blood clot present in

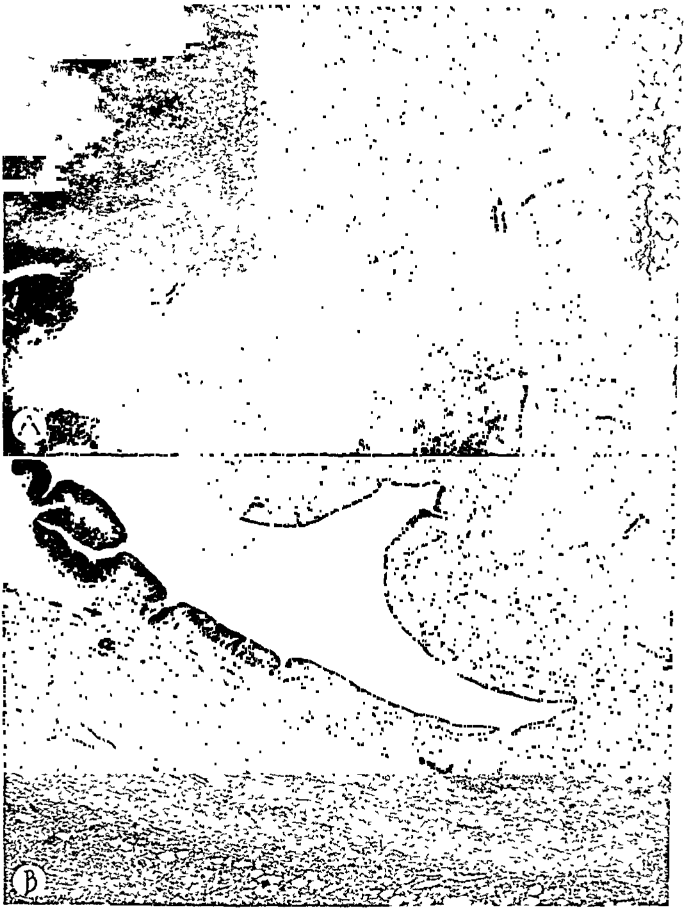

FIG. 2 Photomicrographs. A, renal vein showing vein wall and occlusion of vessel by adherent and organizing thrombus. B, renal pelvis showing extreme passive congestion with submucosal hemorrhage into tissue.

the renal vein, including its main branch (fig. 2, *A*). The calyces and pelvis were filled with blood clot of varying age. The mucosa and submucosa showed much reaction to this. There were many acute inflammatory cells and also phagocytes with blood pigments. A similar reactive inflammation was present in the fat surrounding the entire kidney as well as that within the hilus. The kidney structure was hyperemic and hemorrhagic in areas. Submucosal hemorrhage was present with absence of mucosa in some areas (fig. 2, *B*). The glomeruli were relatively bloodless and the tubular epithelium showed a mild degree of degenerative change of an acute type. All cultures from the kidney were negative.

SUMMARY

The pathology of thrombosis of the renal vein in children and in adults has been reviewed briefly and a case of thrombosis of the renal vein in an adult with recovery presented. The diagnosis of hemorrhagic infarction of the kidney due to venous thrombosis can easily be overlooked clinically. The treatment in unilateral cases is nephrectomy as early as possible.

The Journal of Urology
Vol 75 No 5 May 1956
Printed in U S A

ACQUIRED RENOCOLIC FISTULA IN REMAINING FUNCTIONING KIDNEY WITH RECOVERY CASE REPORT

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The subject of renocolic fistula is still characterized by confusion The occurrence of a fistulous communication between the kidney and any adjacent structure has always presented a formidable diagnostic and therapeutic problem In this respect those that involve the kidney and colon are equally so

In view of the confusion, relative rarity, especially of those showing communication between kidney pelvis and colon and the associated high mortality, as well as the diagnostic and therapeutic problems incident to them, it is proposed to briefly review that portion of the literature dealing only with renocolic fistulas and to report one additional case occurring in a solitary functioning kidney, correctly diagnosed by pneumonephrosis and barium enema, successfully managed without nephrectomy, and presenting a number of the unusual features of the entity, including a direct communication between kidney pelvis and colon.

INCIDENCE

Others have already commented on the favorable reduction in incidence of this lesion during the past half century This may be directly attributable to its prevention by better diagnostic and therapeutic facilities leading to the early recognition and treatment of those diseases which usually serve as causative factors responsible for this complication when undiagnosed or untreated One would predicate an increased incidence of such lesions on a traumatic basis as an aftermath of the war Their failure to materialize in the literature to date may ultimately stand as a tribute to the high grade surgical care given these men in the recent conflict

HISTORY

Hippocrates in his Opera Omnia written in about 460 B C made reference to the surgical management of spontaneous renal fistulas associated with calculi It is presumed that he here dealt with that group which Abeshouse has included under his classification of cutaneous fistulas Rayer in his classical monograph on diseases of the kidney published over a century ago has been given credit for developing the subject at considerable length

In limiting our discussion to those of renocolic type it should be pointed out that more recently Vermooten and McKeown were able to collect 26 cases before 1933, only two of which represented a communication between kidney pelvis and bowel In 1935 Mertz collected 29 cases and added two personal ones and in 1946 Miller reported an additional one and was able to bring the total to 39 cases

Accepted for publication December 15, 1955

ETIOLOGY

Abeshouse, writing in 1949, was able to collect a total of 89 authentic cases, none of which were traumatic or neoplastic in origin and only one of which was associated with a ruptured hydronephrotic sac that complicated a ureteral stone. In his etiological analysis of these it is evident the great majority arise from renal tuberculosis (25 cases); calculous pyonephrosis (23 cases); and uncomplicated pyonephrosis 12 cases. He notes only two with associated pneumopyonephrosis and one with ruptured hydronephrosis complicating a ureteral stone.

Renocolic communications are generally agreed to represent a complication of a pre-existing suppurative process. They may be etiologically classified as follows:

1. Spontaneous
    - A. Renal origin
        - 1. Calculus with or without obstruction
        - 2. Infection due to plant and animal parasites
            - a. Tuberculosis
            - b. Nonspecific bacterial
            - c. Echinococcosis, actinomycosis, bilharzia, etc.
        - 3. Neoplasm (not reported to date)
        - 4. Congenital renal defects
    - B. Extrarenal origin
        - 1. Extrarenal infection, specific or nonspecific involving adjacent viscera and musculoskeletal system.
        - 2. Neoplasms
2. Traumatic
    - A. Crushing or penetrating
    - B. Operative

To date no renocolic fistula due to neoplasm or to associated primary disease in the bowel has been found reported in the literature.

Vermooten and McKeown noted that of their 26 cases only two represented a communication between kidney pelvis and bowel and that the remaining 24 cases were between calyx and bowel. In this regard they stressed the anatomical relationship of the anterior surface of the kidney to the large bowel noting that the large bowel makes direct contact with the lower one-third of each kidney with more extensive contact on the right. No peritoneum is interposed in these areas.

These same authors have noted Rayer's rather classic description of the symptomatology as outlined in his "Traite des Maladies des Reins et des Alterations de la Secretion Urinaire" written in 1839. They apparently concurred in Rayer's idea that a long period of antecedent chronic inflammation of the kidney and perinephritis was the essential forerunner of the fistula. It was presumed that this period was essential to the formation of sufficient fibrous adhesions to adhere the kidney to the colon, and ultimately to necrose the wall, rather than to break through the dense perirenal adhesions. These writers considered this the explanation of the fact that the great majority of these fistulas pass through the kidney substance The two exceptions have been those cases of Eugene Fuller and Watson and Cunningham

SYMPTOMS

The manifestations of renocolic fistula are varied, depending upon the primary renal disease, the complicating lesions such as perinephric abscess, and on the duration of the fistula Mertz, likewise, has pointed out that early adherence of the peritoneum and large bowel to the underlying kidney in the presence of inflammation probably explains the insidious development of these fistulas as well as the relative infrequency of associated perinephric abscesses

The initial symptoms and signs are usually those of the primary renal disease Often there is an associated tumor in the flank which disappears suddenly with marked relief of symptoms and with the appearance of pus and urine in the stools With the advent of the inflammatory phase, a picture of extreme sepsis makes its appearance Abdominal symptoms are usually present but not diagnostic Pain, tenderness, rigidity are present in varying degrees Distention of varying degrees is usually present in the more extreme instances This may be confused with peritonitis but, if carefully observed, seldom with intestinal obstruction Nausea and vomiting are the rule Urinary symptoms will vary with the primary renal disease Frequency, dysuria and pyuria are variable Fuller observed pneumaturia in one case Once the communication is established an intractable watery diarrhea with systemic evidence of urine reabsorption may make its appearance The actual passage of urine, pus, and stones by rectum may occur If the diagnosis is long overlooked these patients deteriorate rapidly and become extremely poor surgical risks Preoperative diagnosis is more frequently established with the advent of better methods of pyelography, and colon studies Blood chemistry offers additional indirect aid

TREATMENT

Accepted methods of treatment will require individualization The usual procedure in the past has been a closure of the colon with associated nephrectomy As will be noted later in the authors' case, we were dealing with such a fistula in the one remaining functioning kidney and nephrectomy was not tenable

UNUSUAL FEATURES

The case recorded here is an additional one showing communication between renal pelvis and colon and represents a number of the unusual features of this diagnostic entity It was first of all acute and occurred in a patient with total renal failure on the opposite side due to a large obstructing ureteral calculus The diagnosis was initially suggested by one of us (D C) from the x-ray evident pneumonephrosis and confirmed by barium enema It represented one of the group of ruptured hydronephroses complicating ureteral stone but with secondary perinephric abscess formation The symptom complex was classic including renal colic, abdominal symptoms, extreme sepsis, uremia, and uncontrollable diarrhea secondary to the pyourinary drainage. Surgical recovery was complete without nephrectomy.

CASE REPORT

A 64-year-old white man was first seen in the home by one of us (C. E. K.) on February 3, 1953 complaining of steady, boring pain in the right upper abdomen, right lumbar area and radiating to both testicles. This pain was of 24 hours' duration having had a gradual but progressively more severe course. Hiccoughing was prominent in the picture and remained a severe complication throughout the illness. Black vomitus followed the onset of the hiccoughs. A diagnosis of right nephrolithiasis had been made elsewhere in 1938. Twenty-four hours later the right upper quadrant pain recurred and a large, tender mass was first noted in this area. Distention was severe, but peristalsis was audible. Hospitalization was refused.

Four days after the onset the patient was again seen because of extreme hiccoughing; again hospitalization was refused. The findings were essentially unchanged except for some diminution of tenderness. A flat film of the abdomen revealed a slightly distended right kidney; the left was poorly outlined. There were radiopaque shadows over both the upper and lower ends of the right ureter and a large, similar shadow superimposed in the region of the left midureter.

On February 9, excretory urography revealed a grossly distended right renal collecting system with minimal dye excretion and poor visualization of the left. All three shadows were thought by the radiologist (D. C.) to be ureteral in location. Retrograde pyelography the following morning revealed obstruction of the right ureter 5 cm. above the ureterovesical junction and of the left ureter at 20 cm. above the ureterovesical orifice at which levels the previously noted calculi were positively identified.

February 15, 1953, the patient finally consented to hospitalization because of severe penile pain. A roughly irregular calculus measuring 1.5 by 1.2 by 0.6 cm. was extracted from the urethral meatus. This calculus represented the one previously noted in the lower right ureter.

Urinalysis revealed cloudy, alkaline urine with specific gravity of 1.011, 2 plus albumin, negative sugar and 20 to 25 white blood cells per low power field uncentrifuged. Blood urea nitrogen was 43 mg. per cent. Hemoglobin was 13.8 gm. with a white blood cell count of 30,600 in a moderately dehydrated patient. Four days later clinical jaundice was evident, progressed to a deep jaundice in 48 hours and continued thus for 10 days. Blood urea nitrogen reached 55.5 mg. per cent. February 27, large, yellow, liquid stools began and remained almost uncontrollable until surgery 1 month later.

March 10, 1953, right pneumonephrosis was evident on x-ray examination (fig. 1, *A*). Barium enema revealed almost complete filling of the right side of the genitourinary tract including renal pelvis, ureters and bladder (fig. 1, *B*). It was believed that the fistula extended from the ascending colon to the upper ureter.

April 1, 1953, right ureterolithectomy with closure of a renocolic fistula was completed. At surgery the previously noted upper ureteral calculus was found

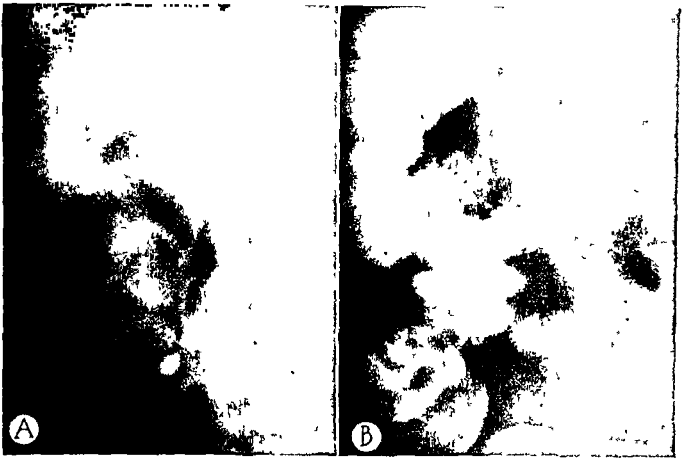

FIG. 1. A, pneumonephrosis showing stone in right upper ureter. B, barium filled right kidney pelvis and ureter. Abscess cavity and communication with ascending colon are evident as is one of the stones.

to have eroded through the wall and was found lying immediately adjacent to the ureteropelvic junction. A communication from the pelvis of the kidney arising at this junction extended into a 30 cc abscess cavity and from thence into the upper limits of the ascending colon. Marked inflammatory reaction and dense fibrotic scarring were encountered throughout the procedure. The defect in the posterior wall of the ascending colon was closed and the ureteropelvic junction reconstructed over the arm of a T tube inserted in the ureter below this level.

The postoperative course was uneventful except for minimal evidence of fecal drainage from the wound from the third to the sixth postoperative day. The blood urea nitrogen had dropped to 11 mg. per cent by the fifth postoperative day.

The T tube was removed 4 weeks later and the anastomotic site dilated from below 5 months later.

Improvement in general health, in kidney function and in weight was almost phenomenal. The patient still refused to have any consideration given to improvement of the situation known to exist on the left side.

November 11, 1954, the patient suffered severe posterior coronary occlusion for which adequate care was again refused. He died 9 days later of a ruptured myocardium.

At autopsy all clinical diagnoses were confirmed.

Probably the most significant necropsy finding was the extreme degree of dense perinephric fibrosis found bilaterally. Sharp dissection was required to remove each kidney from its bed. The right kidney parenchyma, pelvis and ureter appeared normal. The left presented a shell of minimal functioning capacity with a 3.5 by 1. by 0.8 cm. impacted calculus in the upper ureter.

The colon presented only a 1.0 cm. area of scarring approximately 7 cm. above the ileocolic junction and was otherwise essentially normal.

SUMMARY

Renocolic fistula as one phase of the more inclusive subject of renovisceral and renocutaneous fistula has been considered and the literature briefly reviewed.

The symptomatology and treatment have been summarized and a mortality rate of over 30 per cent noted.

A simplified etiological classification is presented. It is noted that no renocolic fistula due to neoplasm or to associated primary lesion in the bowel has been reported in the literature.

A case occurring in the one remaining kidney of function, treated surgically and cured without nephrectomy, has been presented. The statistically unusual features of this case are noted as well as the fact that diagnosis was first suggested by the x-ray evidence of pneumonephrosis.

Death followed acute coronary thrombosis and a subsequent rupture of the myocardium 21 months after onset of the fistula.

Necropsy was especially significant in its demonstration of the extreme degree of perirenal fibrosis alluded to in the literature and previously referred to in the text of our case report.

Our patient apparently brings the total reported cases of this entity to ninety, eighty-nine having been previously collected by other authors.

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The Journal of Urology
Vol. 75, No. 5, May 1956
Printed in U.S.A.

BONE FORMATION IN THE URETER: A CASE REPORT

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Extraskeletal or heterotopic bone formation is known to occur in the urinary tract primarily under two sets of circumstances. The first is the deposition of the bone in the bladder wall and in abdominal wall scars following operations on the bladder and prostate gland.[1-3] The other is the experimental induction of bone formation when a section of epithelium of the urinary tract is transplanted to suitable portions of the parietal connective tissue or fascia. The latter was demonstrated by both Neuhof[4] and Huggins.[5-8] The spontaneous appearance of bone in the human ureter is rare. The present report deals with such a case. There are no similar instances recorded in the literature.

CASE REPORT

A 26-year-old married woman was first seen in 1953. Her chief complaint was recurrent left flank pain of approximately three years' duration. The attacks of pain were sometimes accompanied by burning on urination. No previous urological studies had been done. Examination at the time of the first visit disclosed only some tenderness over the left kidney. A catheterized specimen of urine showed innumerable pus cells. A plain film of the urinary tract showed a cylindrical shadow with a calcified rim in the course of the left ureter suggestive of a ureteral calculus at the level of the fourth lumbar vertebra. An excretory urogram showed prompt excretion and normal outlines on the right side. On the left excretion was delayed. The calyces and pelvis were dilated. The left ureter was not outlined. A cystoscopic examination showed a normal bladder. The ureteral orifices were normal. A ureteral catheter was passed through the left orifice for a distance of 12 cm. easily. However, it could be advanced no farther. An x-ray indicated that the tip of the catheter was at the lower edge of the shadow observed in the plain urogram. The patient was advised to enter the hospital for further study. A second urinalysis again showed pus cells and E. coli grew on culture. Studies for acid-fast organisms were negative. Hematological and blood chemistry studies were normal. Cystoscopy and catheterization of the left ureter were repeated,

Accepted for publication January 11, 1956.

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with the same result as previously. Contrast medium injected through the ureteral catheter passed around the tip of the catheter and down the ureter. No dye was visible beyond the obstructing object. On the supposition that we were dealing with some type of obstructing ureteral calculus, albeit an odd looking one, operation was advised and performed. The ureter was approached through the customary flank incision, identified, and isolated without difficulty. For a short distance surrounding the obstruction there was a pronounced ureteral and periureteral reaction consisting of thickening and induration of the ureteral wall and the periureteral areolar tissue. These findings were thought to be consistent with the localized ureteral and periureteral reaction commonly seen at the site of a calculus. The ureteral wall over the "calculus" was incised and the customary grating sensation noted as the knife's edge came in contact with the stone. However, considerable difficulty was encountered in freeing the object from the wall of the ureter. Its liberation was finally accomplished and it was delivered. It had a cylindrical form and a dense cartilaginous texture. Its true nature was unsuspected at this time. A catheter was passed easily to the renal pelvis then to the bladder. The ureteral incision was then closed with several sutures approximating the edges loosely. A Penrose drain was inserted at the site of the ureterotomy and the wound closed in the customary manner.

Pathologist's report (Dr. David Spain): The specimen consisted of a bony hard piece of tissue that measured 0.5 cm. in diameter at its widest point. Micro-

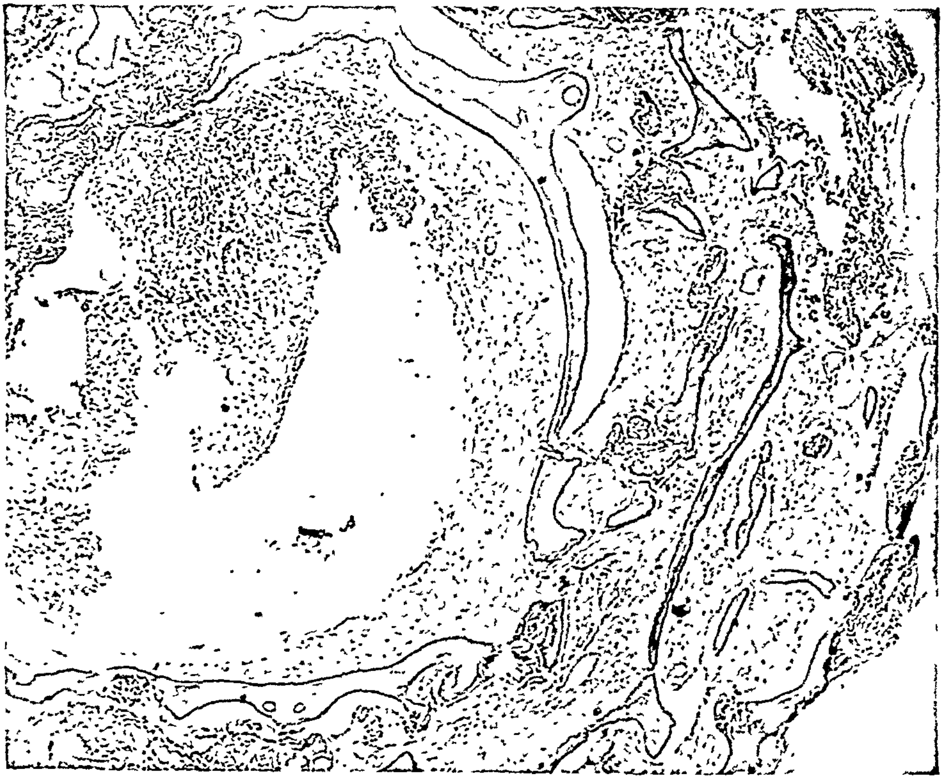

FIG. 1

scopically it consisted of an irregular arrangement of fully formed bony trabeculae with fat tissue and marrow filling in the spaces

Figure 1 represents a photomicrograph of the sectioned specimen, and in it one can clearly see bone and bone marrow elements

The convalescence was uncomplicated except that urine continued to drain from the wound beyond the time when it normally would have been expected to cease Accordingly, another cystoscopy was done and an attempt made to catheterize the left ureter The catheter met an obstruction at the same point as preoperatively, indicating, apparently, that healing by scar had taken place with resultant occlusion of the ureteral lumen Within several days after this procedure, however, drainage suddenly stopped With the cessation of drainage there was no pain, no fever, no palpable enlargement of the kidney and no mass in the operated region It was presumed that the left kidney had ceased functioning Confirmation was obtained by means of an excretory urogram which showed no dye in the left kidney even after long delayed exposures Furthermore the renal shadow was not enlarged The patient was informed that re operation was advisable and that nephrectomy was a possibility However, since she was completely asymptomatic at the time and continued to remain so to the time of writing, she steadfastly refused Subsequent urographic studies showed no change in the kidney's status and repeated attempts to catheterize the left ureter were fruitless

This case is presented principally because it is a medical curiosity Had the true nature of the lesion been recognized at the time of operation, the management would have been different A more satisfactory end result doubtlessly would have been obtained had the entire segment of the involved ureter been excised and an end-to end ureteral anastomosis done

It is interesting to speculate as to how this bone deposition occurred That ureteral mucosa can induce the formation of bone under experimental conditions is known Normally it does not, of course, cause its adjacent connective tissue to undergo such metaplasia However, it is conceivable, in the present case, that under the abnormal influences of infection and irritation, conditions akin to the experimental ones were present, and under such circumstances bone formation in the subepithelial tissues was possible, and did, in fact, occur

SUMMARY

A case of bone formation in the ureter of a patient mistakenly thought to have a ureteral calculus is presented

The explanation for this unusual finding probably lies in subepithelial metaplasia under the influence of the ureteral mucosa in an abnormal environment of infection

Surgical removal of the object was followed by ureteral occlusion and apparently autonephrectomy.

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The Journal of Urology
Vol 75, No 5, May 1956
Printed in U.S.A.

URETERAL REGENERATION FOLLOWING EXPERIMENTAL SEGMENTAL RESECTION

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Since Davis[1,2] first reported the successful results of intubated ureterotomy for the treatment of ureteral stricture, there has been renewed interest in ureteral regeneration. At the time our study was undertaken, Davis,[1,2] Kimbrough,[3] Lapides,[4] and Boyarsky and Duque[5] had reported on the ability of the ureter to regenerate itself over a splinting tube after partial resection of its circumference. It was found that epithelial proliferation was well under way within four days and complete within three weeks. At this time the muscular coat was 50 per cent complete, and after six weeks 90 per cent complete.

Because of this facility of the ureter to regenerate itself after partial resection, and stimulated by the fascinating work of Bohne[6] on bladder regeneration over an acrylic mold we became interested in determining the regenerative capacity of the ureter after complete removal of a segment with no attempt to bridge the defect except by an interposed polyethylene tube. If significant regeneration would occur after prolonged intubation ureteral substitutes or urinary diversion for handling large ureteral defects might be unnecessary.

MATERIAL AND METHODS

Eight healthy mongrel dogs of both sexes, weighing between 10 and 12 kilograms, were used in this study. Under intravenous pentobarbital anesthesia with the animals on their right side, the left ureter was exposed by a flank incision which was extended caudally to the inguinal region. The peritoneal cavity was entered and after walling off the abdominal contents, the parietal peritoneum was opened posteriorly, exposing the ureter. Five to six centimeters of the midureter were then excised, and the defect splinted by a 6F polyethylene catheter which extended distally into the bladder.

In the first two animals the splinting catheter was threaded through an opening in the pelvis down the proximal ureter, and after bridging the experimental defect was passed through the distal ureter into the bladder. After hydronephrosis

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Read at annual meeting, North Central Section of American Urological Association, Chicago, Ill. September 29–October 1, 1955.

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was seen to develop in these first two animals, the remainder had a nephrectomy at the time of creation of the ureteral defect The proximal ureter and the splint were fixed without distortion to the underlying musculature by one or two silk sutures In the course of the nephrectomy, the vessels were ligated as close as possible to the renal substance The ligature was placed about the renal artery distal to the origin of the vessel supplying the ureter The renal pelvis was coned out of the hilum in an effort to employ as much proximal ureteral and pelvic length as possible After the splinting catheter had been effectively placed, the area was reperitonealized with interrupted black silk sutures attempting to cover the defect with retroperitoneal fat The abdomen was then closed following the experimental procedure The animals were sacrificed at intervals varying from three to six months The bladder and ureter, including the splint were removed in toto, examined grossly and fixed in formalin After fixation, sections of the proximal, distal and mid defect were taken for microscopic study Where indicated, special connective tissue stains (van Gieson) were employed

RESULTS

The results are summarized in table 1 As previously pointed out, hydronephrosis developed in two animals in which the kidney was not removed In six of the animals the defect could be grossly identified by a thin attenuated region of connective tissue In the other two animals (Nos 6 and 8) there was marked scarring and distortion of the resected ends In animal No 4 there was calculus formation about the lower end of the splinting catheter as it projected into the bladder In the first two animals where the kidney was not removed, the lumen of the splinting tube was occluded by precipitated urinary crystals

TABLE 1

Animal	Observation Period	Gross Findings	Microscopic Findings
	mos		
1	4	Marked hydronephrosis Connective tissue bridge	No regeneration of muscularis Epithelium lost
2	3	Marked hydronephrosis Connective tissue bridge	No regeneration of muscularis Thin epithelium
3	6	Connective tissue bridge	No muscularis Heteroplastic bone Thin epithelium
4	5	Calculus about ureteral splint Connective tissue bridge	No muscularis Irregular epithelial hyperplasia
5	4	Lower ureteral dilatation Connective tissue bridge	No muscularis Epithelium lost
6	3½	Marked scarring and distortion	No muscularis Severe inflammation Heteroplastic bone Thin epithelium
7	3	Connective tissue bridge	No muscularis Scanty epithelium
8	3	Marked scarring and distortion	No muscularis Heteroplastic bone Thin epithelium

Microscopically, there was no evidence of smooth muscle regeneration. Representative sections (fig. 1) show the microscopic findings of the proximal, distal and midportion respectively of the area of resection in one animal.

Typically, the resected ends with their smooth muscle coats were lost in scar

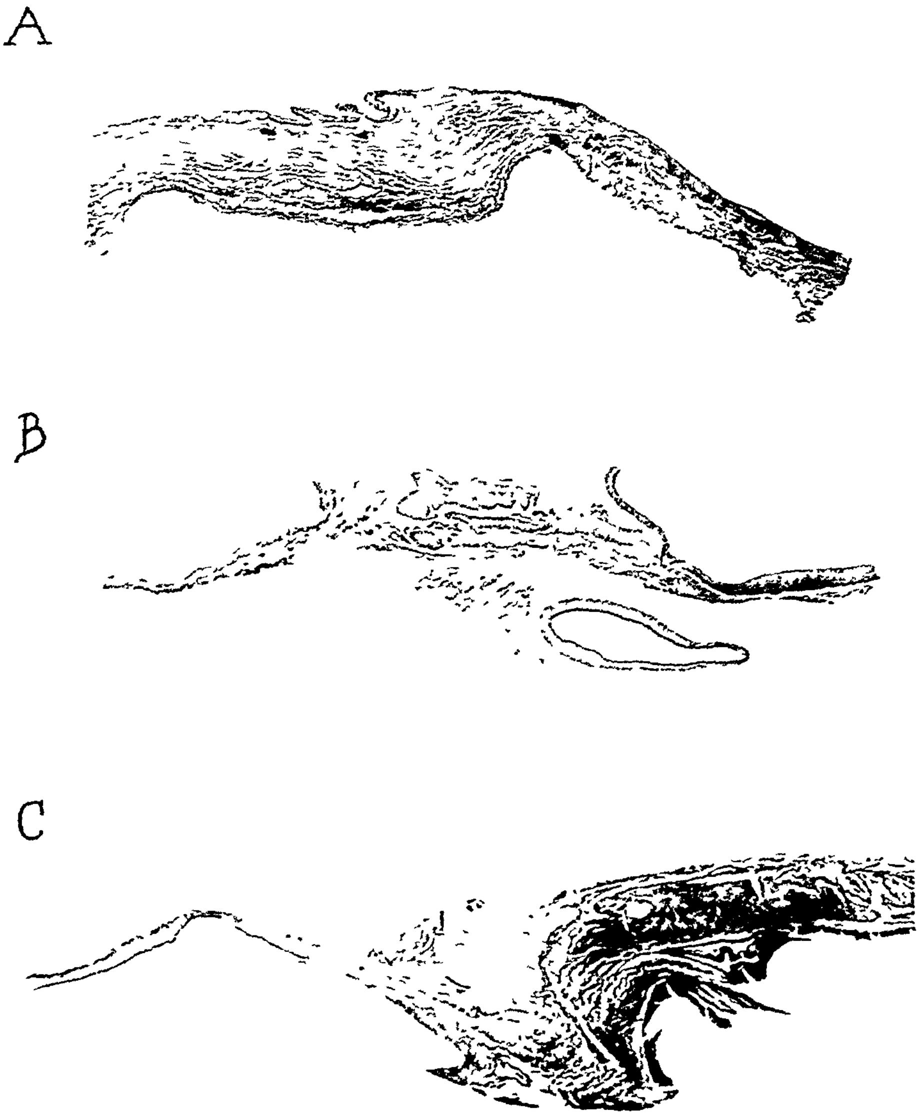

Fig 1 A, longitudinal section of proximal resected end and proximal section of regenerated connective tissue at area of defect Heteroplastic bone is seen as dark islands beneath epithelium × 11

B, longitudinal and cross-section (lower) of midportion of resected area. Dense area at midportion of longitudinal section is cicatrix. Loss of continuity of epithelial surface is an artefact of processing. × 11

C, longitudinal section of distal resected end and distal section of regenerated connective tissue at distal area of defect × 11 tissue which bridged the defect When the epithelium regenerated, it was usually in a comparatively thin layer (fig 1) and occasionally it appeared as simply a hyaline membrane In one animal (No 4), there was hyperplasia of epithelium In three instances (fig 1, A) heteroplastic bone formation was noted

DISCUSSION

The failure of muscle regeneration and the presence only of a connective tissue tube which itself is likely to stricture after removal of the splinting catheter make this procedure impractical for overcoming total ureteral defects It seems likely that the results in humans would parallel those found here Scher, Erickson, and Scher,[7] in a group of dogs used a polyethylene tube for a prolonged period as a permanent prosthesis During their period of observation no significant hydronephrosis developed contrary to our experience in dogs 1 and 2 They likewise found a connective tissue tube to encircle the prosthesis but did not report the degree of mucosal or muscle regeneration

Although crystallization did occur within the lumen of the tube in some of our cases, polyethylene and closely related substances appear still to be the least reactive of recently developed plastic materials This has been shown experimentally and clinically in a wide variety of substitutive procedures The presence of crystallization might be related to bacterial infection which we made no attempt to determine Herdman[8] used polyethylene as a ureteral splint in rabbits and found occlusive crystallization with great frequency, enough so that he dismissed the substance as unsatisfactory It seems certain that when the material is used in the urinary tract precipitate will occasionally be encountered

The failure of the ureter to respond in a fashion comparable to the bladder in regenerative capacity is interesting and at the same time perplexing The presence of transitional epithelium because of its recognized regenerative ability was anticipated The proliferation of fibroblasts to form a connective tissue tube has been demonstrated by Scher[7] and shown by Bohne[6] about the acrylic mold Because of the absence of muscle fibers in our findings one wonders whether there is any basic difference between the smooth muscle cell of the ureter and bladder and whether tissue culture studies would reveal any change in the inherent regenerative capacities of the cells of these two structures If smooth muscle regeneration occurs as a result of the simple mitoses of pre existent smooth muscle cells one might expect to find regeneration near the transected ends of the ureter, there was no evidence of this Because of the absence of regrowth of smooth muscle from the ureteral ends it seems unlikely that the bladder muscle regeneration demonstrated by Bohne occurs from the divided urethra and ureters However, it is possible that with a still longer period of splinting muscle fibers might be demonstrated We hope to explore this possibility further in subsequent experiments

In support of a possible tissue difference in regenerative capacity is the recent work of Berman[9] who used a polyethylene substitute for the esophagus. He likewise could not demonstrate any smooth muscle regeneration and also found the prosthetic tube to be surrounded by epithelium and connective tissue.

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[8] Herdman, J P Polyethylene tubing in experimental surgery of the ureter Brit J Surg , **37** 105, 1949

Heteroplastic bone within the connective tissue layer adjacent to the mucosa of the splinted portion was found in dogs No. 3, 6, and 8. Huggins[10] has shown that proliferating transitional epithelium has a peculiar influence upon certain fibrocytes to convert them to osteoblasts and hence form new bone. Although bone has been shown to occur in many organs subsequent to injury and inflammation we believe that in these dogs the regenerating transitional epithelium is the underlying factor.

CONCLUSIONS

In a series of 8 animals after the creation of a total ureteral defect, muscle regeneration could not be demonstrated about a splinting polyethylene tube for periods up to 6 months. Because of this failure to satisfactorily bridge a total ureteral defect various other types of substitution procedures still remain a clinical necessity.

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THE JOURNAL OF UROLOGY
Vol 75 No 5 May 1956
Printed in U S A

DERMOID CYSTS OF THE BLADDER

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Primary dermoid cysts of the bladder are exceedingly rare, and ovarian and paravesical dermoid tumors communicating with the bladder are not common

In 1895 Clado collected 32 cases of paravesical dermoids from the literature, in eighteen of which hair was passed in the urine Since then there have been isolated reports (almost all in the foreign literature) of but single cases Because secondary dermoid cysts (ovarian in origin) greatly outnumber primary ones, the sex incidence in the reported cases has been largely in females

The most characteristic symptom in cases of dermoid cysts of the bladder is pilimiction which was first described by Wallace in 1700 Less often calculi and sebaceous material and rarely teeth may be passed in urine Other symptoms are entirely nonspecific and consist of frequency, dysuria, pain, obstruction to the flow of urine, and hematuria

The following is a case report of a dermoid cyst of the bladder

D K, a 30-year old white woman, was first seen by her family physician in July 1953, for pain at the end of urination She gave a history of voiding every three to four hours with no dysuria, burning or smarting, but would occasionally pass what looked like granite out of a tea kettle At times this seemed to have hair attached to it Rare terminal hematuria was present but no urgency Nocturia two to three times per night was present

She saw her family physician one to two times a week after that time, and stated that at one time her urine was clear but that most of the time it was cloudy and contained pus Her symptoms gradually became worse and excretory urograms were ordered in September 1954

Study of the films resulted in a diagnosis of multiple calculi of the bladder (fig 1) I was asked to remove them It was my impression after examining the films that if the opacities present were calculi they must be in multiple diverticula of the bladder

Laboratory findings were within normal limits except for many pus cells in the urine

On September 9, 1954 a cystoscopic examination was performed Large greyish flakes of calcium were seen floating in the bladder, and a large greyish, whitish mass, with hair and calcium incorporated, seemed to be attached to the left superior bladder wall A few hairs were removed by cystoscopic forceps but the large mass could not be dislodged My first impression was that the patient had probably introduced hair into the bladder, causing a foreign body calculus

Suprapubic cystotomy was performed and the mass, five to six cm in diameter, with hair, teeth and calcium was found to be extending through the bladder, and be firmly attached to two tags of epiploic appendices and very loosely attached to the left ovary The ovary was peeled free easily and was normal in

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Read at annual meeting, North Central Section of American Urological Association, Chicago Ill September 29–October 1, 1955

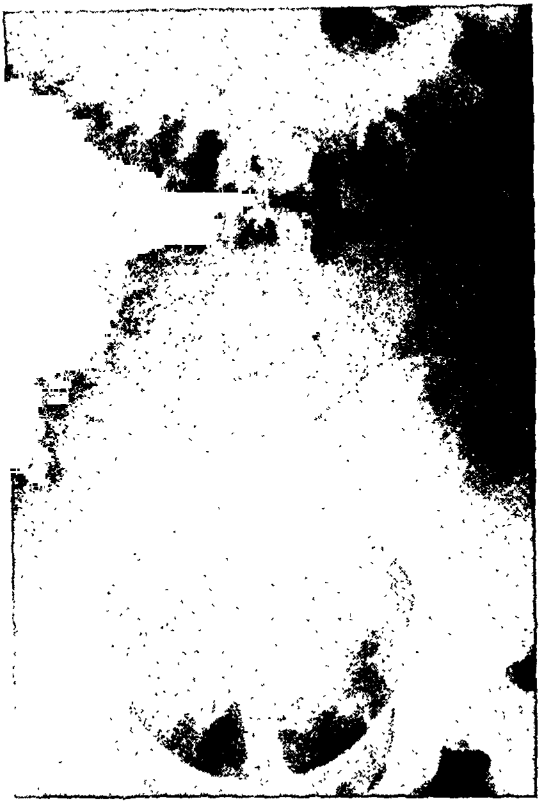

FIG. 1

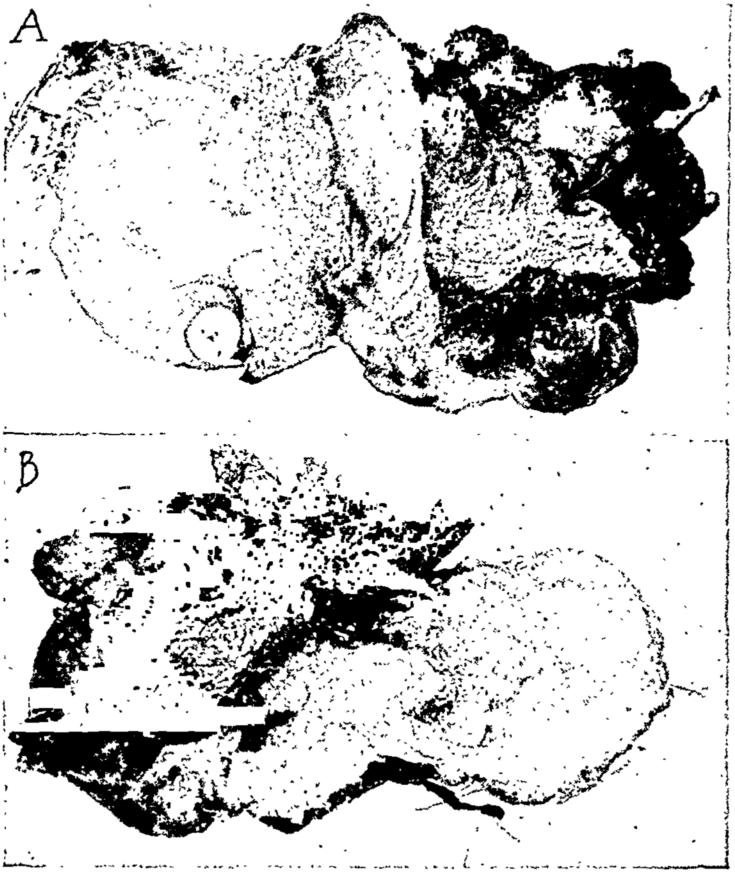

FIG. 2

appearance. Segmental resection of the mass was performed and the bladder closed with suprapubic and urethral drainage. Convalescence was uneventful.

Urine culture showed E. coli present.

Pathologist's report: "Specimen consists of a tumor removed from the bladder by the abdominal route (fig. 2). A cuff of bladder wall is identified and the tumor mass seems to extend through it, protruding internally a distance of 5 cm. A portion of the tumor seems to extend into the perivesical fat. The tumor is composed of obvious skin, hair, teeth, bone and subcutaneous tissue and grossly resembles a dermoid cyst. Its precise origin cannot be grossly determined from gross examination of the specimen.

"First section studied is of urinary bladder alone. Lining epithelium seems to be almost ulcerated in some areas with both an acute and chronic submucosal inflammatory reaction associated with some submucosal hemorrhage. Focal collections of lymphoid tissue are clearly evident in our section and certainly there is edema leading to thickening of the submucosa. The underlying bundles of smooth muscle show their usual loose configuration and there are foci of mononuclear cells infiltrating herein. The serosa, subserosa and perivesical tissues show an intense inflammatory reaction with both acute and chronic elements

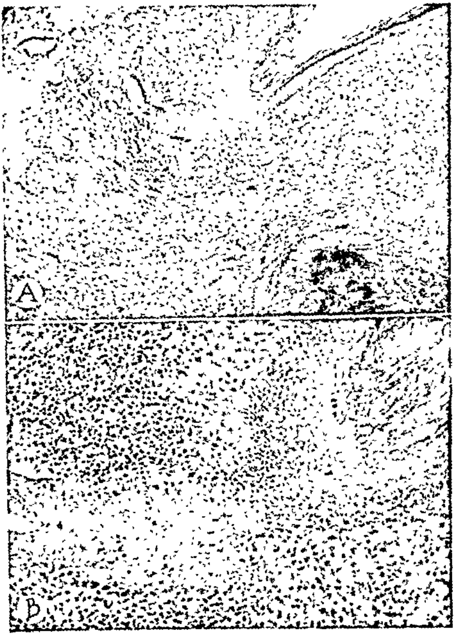

FIG. 3

present and with a considerable foreign body giant cell reaction accompanying the inflammatory process. Another section shows the urinary bladder again with the intense inflammatory reaction as described and the lining transitional epithelium of the bladder in this section seems to pass over and blends with what is obviously keratinized stratified squamous epithelium covering this dermoid tumor. In the depths of the dermoid we can identify nerve tissue with much glial fibrous proliferation and with what seems to be an appendable lined miniature ventricle. Possibly a hodge-podge of other ectodermal tissues may be present and again there is the same serosal and perivesical inflammatory reaction as already noted. In this section we note, at least in part of it, a distinct separation of bladder from tumor but as one proceeds toward the bladder lumen there seems to be a fusion of the tissues of the dermoid and the tissues of the urinary bladder and as previously noted, we find the mucous membrane of bladder and dermoid to blend, one with the other. Sections from the tumor, itself, show that much of it is of central nervous system makeup with associated hair, sebaceous glands and skin. No ovarian tissue is evident in our multiple sections and there does seem to be considerable hair with what appears to be supporting fibrous tissue in the perivesical fat with extension of this dermoid process directly into the urinary bladder. No malignancy of any of the tissues of this dermoid is noted. Diagnosis: 1) Dermoid tumor (teeth, skin, hair and central nervous system tissue) growing into the urinary bladder—origin ovary?, pelvic tissues?; 2) acute exacerbation of chronic cystitis with cystitis granularis and with inflammatory involvement of perivesical tissues" (fig. 3).

SUMMARY

A case of dermoid cyst of the bladder has been described. Definite origin cannot be determined but it is the author's opinion that this arose primarily in the bladder.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
Printed in U.S.A.

JOHANSON URETHROPLASTY FOR REPAIR OF URETHRAL STRICTURES

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Operative repair for stricture of the urethra is not a new surgical procedure. Dugas, in 1836, reported the first case of complete resection of the urethra for the repair of a stricture. It was treated postoperatively by an indwelling catheter without any attempt to suture the ends together. Many other urethroplasties have been devised since then, but are useful mainly in short strictures. The major premise of these techniques is to dissect free and excise all involved scarred urethra and surrounding tissues, and then, a direct end-to-end anastomosis of normal tissues is performed. Grafting techniques have also been devised but require followup postoperative dilatations for an indefinite period.

The Johanson type urethroplasty for the repair of urethral strictures is an application of the Denis Browne technique for hypospadias. The original groundwork for this type of repair was done by Duplay as early as 1874, when he sutured buried epithelium around a catheter. G. Marion and J. Perand, in 1942, used Duplay's method for hypospadias repair but modified it by making the constructed canal continuous with the original urethra. Denis Browne, in 1949, presented his method for construction of the urethra in hypospadias. It differed from the above authors in that 1) the buried strip was wider, 2) the strip was left fully intact without any undercutting, 3) the buried epithelium was not sutured over a splinting catheter, and 4) a dorsal relaxation incision was used in all cases.

Johanson, in reviewing the results of Denis Browne, believed that he could use the principle of a buried intact epithelial strip to develop a surgical cure for any type of urethral stricture. It was also his desire to be able to apply the operation regardless of pathogenesis, extent, or degree of severity of the stricture. He was of the opinion that to be a worthwhile operation and an improvement on preceding urethroplasties, no after treatment should be required, especially dilatations. The first stage of this operation creates an artificial hypospadias, but also serves two time honored principles, one, the draining of an infected area, and two, diversion of the urinary stream from this infected area.

In applying the buried intact epithelial tract technique, the following diagnostic criteria, indications, and contraindications were used.

DIAGNOSIS

All patients were studied thoroughly (table 1). Upper urinary tract studies, naturally, were checked by excretory urograms since the introduction of the cystoscope, in most cases, was impossible. The diagnosis of stricture of the urethra as to caliber, length, number, and location was evaluated by olive tip bougies

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Read at annual meeting North Central Section of American Urological Association, Chicago, Ill., September 29-October 1, 1955.

TABLE 1

Name	Age	Caliber		Etio.	Type O.R.		Hospitalization		Complications
		Pre. op.	post. op.		1st	2nd	1st	2nd	
Clinic Patients, Detroit Receiving Hospital									
Leonard J.	38	Acute ret 4F	22F	Gc. 1939	Scrotal flap		4-2-55	6-12-55	7-13—Debridement of granulations. 12-8—Stenosis distal opening. 2nd stage closure 1½ cm.
Isiah B.	47	12F	24F	Gc. 1940	I		6-14-55	8-5-55	Non. funct. rt. kid. I.V.P. Pyuria Rt. neph. 7-26-55
Benphy F.	20	10F	24F	Gc. 1948		II	8-5-54	10-4-54	Uneventful
James T.	32	14F	22F	Gc. 1941	I		8-23-54	5-16-55	Gc. after 1st. stge 3-55
Paul B.	32	4F	24F	Gc. 1939	I		1-10-55	6-13-55	Uneventful
Earl T.	33	12F	24F	Gc. 1938	I		10-11-54	12-30-54	Fistula after 2nd stage. Closed spontaneously
Shermon L. C.	24	Ret. 0	24F	?		II	10-28-54	1-10-55	Uneventful
James B.	50	14F	24F	Gc. Trauma	I		2-4-55	5-26-55	Incontinence pre op. Complete cont. post op.
Grover R.	50	16F	24F	Gc.		II	4-55	6-55	Post II urinary fistula. Closed spontaneously
Lee W.	63	12F	—	Etio. Tb. ?	I		2-14-55	—	Tb. San. Expired miliary tb. 4-20-55
Arnold T.	37	4F	26F	—	I		11-15-54	1-27-55	Voids well
James D.	32	16F	24F	Gc.	I		10-54	—	Sent to Jackson Prison, Jackson, Michigan
Edward S.	33	4F	24F	Gc. 1947	I	II	11-29-54	3-21-55	Post op. hemorrhage 12-18-54. Urethral fistula following 2nd stage. Closure of fistula 6-6-55.
Andrew P.	25	10F	22F	CuSo Gc. 1947	I		11-1-54	1-20-55	Perineal infection
Harvey W.	67	16F	24F	Gc. 1915		II	12-6-54	5-19-55	Practically spontaneous. 2nd stage closure
Fred W.	40	16F	22F	Gc. 1930. 14 prev. Or	I	II	9-20-54	1-17-55	Dissection of perineum 1st stage. Revision proximal end 1-22-54. Urethral fistula following 2nd stage spontaneous closure
George K.	68	10F	24F	T.U.R. Det. Ost. incont.	I		2-7-55	5-2-55	Uneventful, complete continence post op.

William S	70	16F	16F	Straddle injury age 16		II	5-24-55	7-12 55	Required post 2nd stage dilatation
Floyd H	69	0	24F	8-9-55—Periurethral phlegmon Gc	I	II	10-18-54	3-3 55	1st stage radical dissection perineum and Lf orchiectomy 2nd stage and cystolithotomy Urethral fistula closed 1-28-55
Joseph	74	14F	24F	Dil since 1935 periu abs 3 mos previous Gc in youth	Inversion of scrotal flap supra to find proximal urethral		11-11-54	2-16-55	2nd stage 1-29-55 Developed perineal fistula Closed spontaneously
				Private Patients, Providence Hospital Detroit					
Marchello R	57	Filiform 16F	28F	Gc	I	II	7-27-55	9 20-55	False passage into membranous urethra Retention, hemorrhage Rt hydronephrosis 1st deg
Mika S	37	16F	28F	*Congenital stenosis meatus*	Stricture extends to penoscrotal junction		3-14-55	5-24-55	Acute pyelonephritis Acute prostatitis Rt hydronephrosis, 1st deg
Brian R	28	16F	26F	Congenital hypospadias	I		1 18 55	1-18-55	Rt hydronephrosis, 1st deg Recurrent pyelonephritis Recurrent bouts of periurethral abscess

and oblique urethrograms using 30 per cent sodium iodide in a viscid solution of lubricating jelly.

ETIOLOGY

The *etiology of the cases presented includes: a) those mainly due to an old* gonorrheal urethritis; b) one, due to trauma; c) one, postoperative following transurethral prostatic resection; d) one, chemical in origin; e) one, postoperative stricture in a previously repaired hypospadias with repeated periurethral abscesses; f) one, in a congenitally stenosed urinary meatus with resulting dense stricture along the entire pendulous urethra.

INDICATIONS

Our indications for surgery are not so liberal as Johanson's. We believed that any nontuberculous stricture, 2 cm. or more distal to the membranous urethra, *single or multiple, that did not respond to gentle dilatation was amenable to this* type of repair. This includes a large number of patients seen at Detroit Receiving Hospital who return repeatedly with "tight" filiform strictures with large periurethral abscesses and extravasations, typical "flowering pot" perineums. This includes patients whose strictures could not be dilated above 16F without producing either severe pain, profuse bleeding, acute ascending pyelonephritis, or an acute prostatitis. Johanson, on the other hand, does not limit his repair as to location and states that he has excised fistulous tracts and fibrous tissue *en bloc* proximal to the membranous urethra with complete continence following surgery.

CONTRAINDICATIONS

The only contraindication to the procedure is the patient's inability to stand the anesthesia required. One word of caution: do not perform a first stage urethroplasty too soon after an acute periurethral abscess; it is best to wait at least six to eight weeks or until all inflammatory changes have disappeared. We learned the hard way; we encountered severe hemorrhage because the tissues were extremely friable and accurate hemostasis was impossible.

TECHNIQUE

We followed the technique as outlined by Johanson in his original article, and by Flocks and Culp in their book entitled SURGICAL UROLOGY, with minor variations.

The patient is placed in a mild lithotomy position, so that either perineal or suprapubic regions can easily be exposed. The operation is divided into two stages. The first stage varies as to the location of the stricture in the urethra. It may be divided into meatal and those distal to or proximal to the perineal portion of the urethra.

a) In meatal stenoses or strictures which extend down toward the bulb, the incision begins at the meatus and extends to a point at least 2 cm. beyond the strictured area.

b) In strictures distal to the perineal urethra, a No. 26 sound is passed to the involved area No attempt is made to force the sound beyond this point as only undue trauma will result An incision is then made in the midline of the ventral portion of the penis, through skin, fascia, and corpus spongiosum, down to the sound The incision is extended in a distal and proximal direction until at least 2 cm of normal urethra is exposed If there are no draining sinsuses or periurethral abscesses, one need not dissect or excise the scarred urethral mucosa or corpus spongiosum If the stricture is so severe that the proximal end cannot be identified accurately, a suprapubic cystostomy and passage of a sound through the vesical neck down to the stricture site may be performed The skin edges of the penis are then sutured to the edges of the urethral mucosa with 3-0 chromic catgut or 4-0 black silk

c) If the strictured area extends into the perineal portion of the urethra, a flap of scrotal tissue must be inverted to give one enough skin for closure of the urethra in the second stage operation The technique varies, in that an incision is made in the perineum through skin, subcutaneous tissue, central tendon and bulbocavernosus muscle to the strictured area The urethra is divided until at least 2 cm of normal urethra is seen distally and proximally The proximal urethra may have to be identified by passing a sound from the vesical neck to the strictured area In this area, it is very important to excise all fistulous tracts and surrounding scar tissue completely Next, the scrotal skin flap that is to be inverted is prepared This is done by making an incision along the median raphe 3–4 cm long The skin between the inferior point of the scrotal skin incision and the transverse incision in the perineum is freed The dissection is continued until a bridge of tissue is formed that can be inverted and sutured without tension to the normal urethra The edges of the scrotal skin are then sutured to the edges of the incised urethra This forms a funnel shaped external urethrostomy which Johanson states gives a better functioning permanent urethrostomy than the type that is located posterior to the scrotum The perineal incision is closed by approximating the bulbocavernosus muscle, reconstructing the central tendon and closing the skin A *18F Foley catheter* is left indwelling for 3–4 days after this procedure Johanson insists that even if hair bearing areas are inverted, the hair will soon disappear and afford no hazards We do not fully agree in this premise, but perhaps the future will clarify this difference of opinion

The interval between stages varies with the healing powers of the patient and averages from eight to ten weeks The second stage technique is quite universal Urinary diversion should be performed and was done by suprapubic cystostomy in all of our clinic patients while a perineal urethrostomy was performed in all of our private patients A strip of urethra and surrounding skin approximately 2 cm wide, or 75 per cent of the circumference of the urethra desired, is left intact The lateral skin edges of the penis or scrotum are freed for a distance of 2–3 cm so that the skin edges can be approximated over the buried strip without tension A dorsal relaxation incision is made if necessary The skin is closed with interrupted sutures of chromic 3 0 or 4-0 black silk The tension is taken off this suture line by using No 32 wire held in place with lead shot Care must be taken not to draw the tension suture up too tight as the lead shot will cause necrosis of the skin and possibly result in a fistula. The wire sutures are removed on the seventh to eighth day, the black silk on the tenth day if healing appears complete. The patient is allowed to void on the tenth day if the wound appears solid. Many patients in their anxiety to know the results voided as early as the second day.

COMPLICATIONS

In one of our cases, rather severe postoperative hemorrhage followed a first stage operation. As mentioned earlier, we operated too soon after a periurethral abscess; the tissue was very friable and hemostasis difficult. We resorted to perineal pressure dressings and after a period of about five days the bleeding was stopped. We had a total of six postoperative fistulas. Of these, four occurred along the approximation of the skin edges and two were secondary to pressure necrosis from the lead shot. Three of the fistulas closed spontaneously. Three required simple surgical closure with uneventful postoperative course. In one case infection developed at the site of the perineal incision. All of these patients had healing without recurrent stricture formation. Only one patient was a failure as to surgical repair and required postoperative dilatation.

CONCLUSION

The application of the buried intact epithelial tract technique for the repair of urethral stricture after the method of Johanson with certain modifications has been presented. This procedure was used in highly selected cases when conservative treatment either failed or became unbearable. In our hands, it has been very successful, since we have had but one failure. It is our firm conviction that as time goes on and our technique improves, we will attempt a far greater number with a greater percentage of excellent results.

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THE JOURNAL OF UROLOGY
Vol 75 No 5 May 1956
Printed in U S A

INCARCERATED SCROTAL APPENDICITIS

JOHN R HERMAN

Scrotal appendicitis is a rare form of inflammation of the displaced vermiform appendix It has been reported in the literature only four times Numerous articles have described the abnormal position of the appendix and methods of locating it in the abdomen Its position being so variable, one should not be surprised to find it present in hernias, scrotal or otherwise A case will be presented illustrating incarcerated scrotal appendicitis

The vermiform appendix has been described in almost every place in the abdominal cavity and thorax, in the thigh in femoral hernias, in the right and left inguinal regions in hernias of those areas, and in the scrotum in scrotal hernias Babcock[1] portrayed the appendix as found frequently in hernia sacs Watson[2] reported the finding of the appendix alone in the hernial sac as fairly rare His figure was 53 cases in more than 17,000 collected from the literature

Zambrana[3] reported a case of scrotal appendicular abscess, and Keyes[4] found both appendix and cecum in the scrotum Reif[5] described acute scrotal appendicitis in a male infant, and Mulholland et al [6] gave a description of acute scrotal appendicitis in a 6-month-old boy who had bilateral inguinal hernias as well as an umbilical hernia

The anatomy of inguinal hernias extending into the scrotum has been well recounted To quickly review, the pouch like vaginal process of the peritoneum, which extends down into the scrotum preceding the testicle, may not complete the normal developmental plan of involution in the inguinal canal If the processes vaginalis persists and remains open to the tunica vaginalis, it is a ready-made hernia awaiting only the presence of an abdominal viscus If it is still *present, but partially or completely closed as in the hydrocele of the cord, the* same herniating process is invited

Mulholland et al [6] discussed the likelihood that the scrotal appendix, because of its exposed position, is more likely to inflammatory and traumatic changes than the normally located organ Because of this exposed position, one would expect the diagnosis to be readily made However, the acute local symptoms overshadow the abdominal The actual herniation of the appendix is symptomatically unimportant It is only when it becomes involved in inflammatory changes that these local changes make the patient aware that there is serious trouble Then the painful, red, swollen scrotal mass becomes a very obvious source of complaint The differential diagnosis rests between 1) acute hydrocele, 2) hematocele, 3) testicular torsion, 4) strangulated hernia, 5) hemorrhage into a testicular tumor or 6) virus or other types of orchitis or 7) acute scrotal trauma

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Accepted for publication January 11 1956

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In none of the cases reported was the diagnosis made preoperatively and it was not made preoperatively in the following case.

CASE REPORT

Bronx Hospital No. 286724. This was the first admission of this 7-year-old Negro because of a painless swelling in the right scrotum. It was first noted about 2 weeks ago while his mother was drying him after a bath. It had been completely asymptomatic and neither he nor his mother could state when it had first appeared. He had no recollection of trauma or preceding febrile reaction or gastrointestinal upset. He had no symptoms referrable to the genitourinary or gastrointestinal tract.

Physical examination revealed a well developed, well nourished Negro in no distress. His head, thorax and abdomen all were essentially normal. Temperature, pulse and respiration were also normal. There was a nontender, fusiform swelling in the right scrotal sac which was approximately 8 cm. long and 4 cm. wide. This was quite firm although somewhat cystic in consistency. The testicle and epididymis could not be differentiated from the mass. Examination of the mass revealed a small area at the upper pole that transilluminated clearly. The rest of the mass did not. There was no evidence of hernia on cough or straining and a finger could not be admitted into the external ring. There were slightly enlarged inguinal nodes which interfered with palpation of the ring. The staff was divided on the diagnosis between traumatic hydrocele and hematocele. Blood count was 4,200,000 red blood cells, 6000 white blood cells, 84 per cent hemoglobin (12.2 gm.), 72 segs, 20 lymphs, and 6 monocytes. The urinalysis was negative, specific gravity 1.015.

The scrotum was explored under general anesthesia and the operative report follows:

A 4-inch incision was made from the upper portion of the scrotum parallel to the inguinal ligament and was carried down through the superficial fascial layers. After incising the last peritesticular layer, about 10 cc of straw colored fluid escaped. The tumor became slightly smaller. The testicle was identified and appeared normal in size, shape and consistency. The epididymis and spermatic cord were involved in a swelling which was 2 by 4 cm. in size. This mass was cartilaginous in consistency and was felt to be a neoplastic lesion. Grossly, the cut surface was mucinous with some grumous yellow fluid in one portion. The spermatic cord could not be identified as it lost itself in the mass. It was the consensus of opinion that orchiectomy should be done. What was thought to be the spermatic cord structures were freed of their surrounding tissues in the groin and ligated *en masse*, and divided.

The vas deferens was isolated, clamped, divided and ligated. The mass and testicle were removed *en bloc.* A stab wound was made in a dependent portion of the scrotum for drainage and the scrotum was closed in layers. The postoperative diagnosis was supratesticular tumor, either granuloma or epididymal neoplasm. Grossly, the actual disease was not recognized by the surgeons at the table, or by the pathologists in their gross examinations. It was the microscopic examination which revealed the true condition. The pathologist's report follows:

The specimen consisted of a testicle measuring 15 by 15 mm. in size, and a supratesticular mass measuring 2 cm. by 4 cm. The spermatic cord was not identified separately and the testicle appears to be slightly atrophic. The supratesticular mass was a firm, somewhat cystic structure which on cut section was composed of several fused, thin layers, the inner of which was dark blue. The entire supratesticular mass was matted and adherent to the testicle and epididymis. On cut section, two cord-like structures were identified.

Microscopic section through the testis showed an immature appearance consistent with the patient's age. Section through the supratesticular mass revealed that the cystic structure had a thick fibrous appearance, its wall being composed of dense, partly hyalinized, collagenous bundles and numerous blood vessels. In the central portion of this cystic mass was a cross-section of an appendix essentially normal in appearance except for chronic inflammatory reaction and periappendiceal fibrosis. The peritoneum of the appendix was adherent to the thick fibrous wall of the cystic structure and in some places was absent. Adherent to, and encased in the wall of this inflammatory mass, was the spermatic cord which was essentially normal. Diagnosis: Scrotal hernia with incarcerated appendix showing chronic appendicitis and peri-appendicitis. Normal testicle and cord.

Figure 1 is a diagram based on the operative findings and pathologist's report.

The postoperative course was smooth and uneventful. There was no febrile

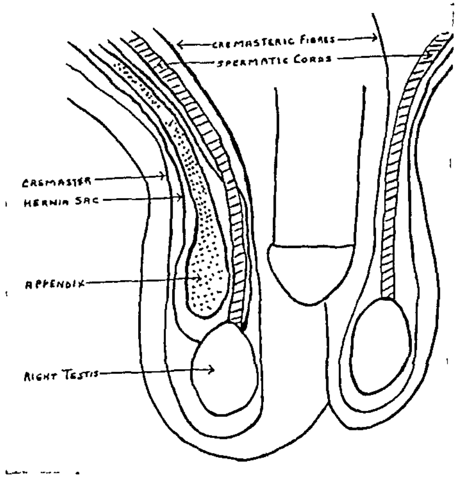

FIG. 1

reaction; the drain was removed in 24 hours, and the boy was ready to go home in 6 days when the report of the pathologist was received. He was held in the hospital one week longer. He has been seen in the clinic and is doing very well. It is intended to readmit the patient to the hospital in 6 months, at which time he will be investigated with a view towards hernial repair and completing the appendectomy.

COMMENT

Scrotal appendicitis, acute or chronic, should be added to the physician's differential diagnosis of scrotal masses. Undoubtedly, there must be more cases of this type that have not been reported. Perhaps a more careful inquiry into the history might reveal gastrointestinal disturbances that could hint towards diagnosis. An awareness of the possibility of this condition might save the physician and the patient from unneeded distress.

SUMMARY

The four previously reported cases of scrotal appendicitis have been briefly reviewed and another case of chronic scrotal appendicitis added. Differential diagnosis has been discussed.

Gratitude is extended to Dr. M. L. Gottlieb, chief of the urological service, and to Dr. Lycourgos Papapadakis, department of pathology.

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THE JOURNAL OF UROLOGY
Vol 75 No 5 May 1956
Printed in U S A

DUPLICATION OF LEFT UNDESCENDED TESTICLE REPORT OF A CASE

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Polyorchidism is a rare phenomenon By 1954 Darrow and Humes could find 22 authenticated cases These authors reviewed the literature and added a case of their own Their case concerned a 23-year-old white man with two testes in the right scrotum Each testis had its own epididymis and vas This appears to be the second example of a double vas (one for each testis), the first instance being represented by Thiessen's case

Two additional cases of polyorchidism were reported in 1954, thus bringing the total to 25 Carey's case was that of a 9 year-old boy with a double testis on the left side They were in the inguinal region and 3 cm apart The lower one was connected with an intact epididymis and vas The upper was apparently without cord structures Waite's case concerned a 19-year old Japanese operated upon for an undescended testis associated with an inguinal hernia on the left side, complicated by incarceration of bowel or omentum At operation two testes were found, the lower one associated with a vas and epididymis, and the upper having an epididymis but no vas

Polyorchidism is practically synonymous with triple testes, since, to the best of our knowledge, no histologically verified cases showing more than three testes have been reported Developmentally, polyorchidism can be explained by splitting of the inner epithelial mass during their development within the genital ridge Failure of one gonad to link up with the wolffian duct might account for the usual feature of one vas deferens serving both gonads The most probable explanation is that the split gonad has at least microscopic continuity with the wolffian duct, but requires careful dissection, and possibly serial sectioning for demonstration

The following case report demonstrates left side duplication of an undescended testis associated with an indirect inguinal hernia Each testis had its own epididymis, but no apparent communication with the vas was found in the case of the lower testis A normal sized testis was found in the right scrotum

REPORT OF CASE

N T, a 15-year old white boy, was admitted to the hospital division of the Medical College of Virginia on June 13, 1955 for repair of an inguinal hernia On physical examination an indirect hernia was found on the left side, as well as an undescended left testicle The right testicle was normal in size and located within the right scrotum Blood count and urine examination were within normal limits Serologic test for syphilis was negative

The patient was operated upon the following day under intravenous surital

Accepted for publication December 5, 1955

sodium anesthesia, supplemented by anectine drip. A skin incision was made beginning at the pubic spine and extended upward in a slightly divergent direction from the inguinal ligament for a distance of 10 cm. The aponeurosis of the external oblique was divided, and the cord, which extended down to the symphysis pubis, was developed by sharp dissection and mobilized. Lying in a supermedial position to the cord, the hernial sac was identified and freed from the surrounding structures. The defect in the peritoneal cavity was then closed by a purse-string suture of chromic No. 1 catgut. The cord was mobilized further, ligated

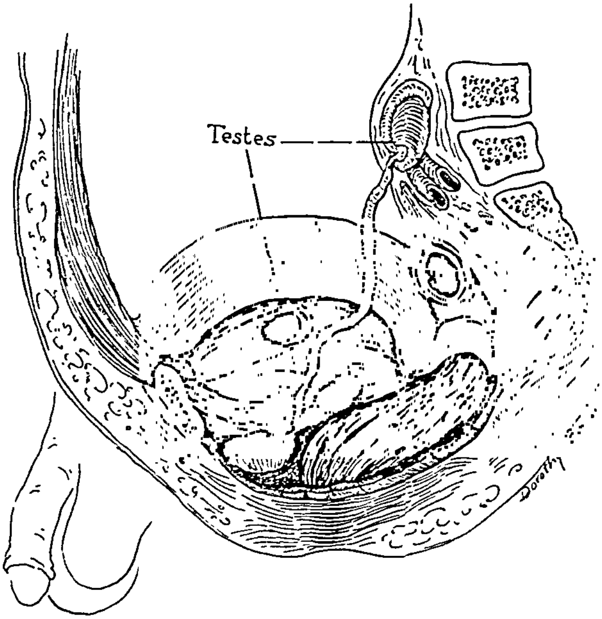

Fig. 1. Artist's conception of operative findings prior to removal of testes and vas deferens. Parasagittal view.

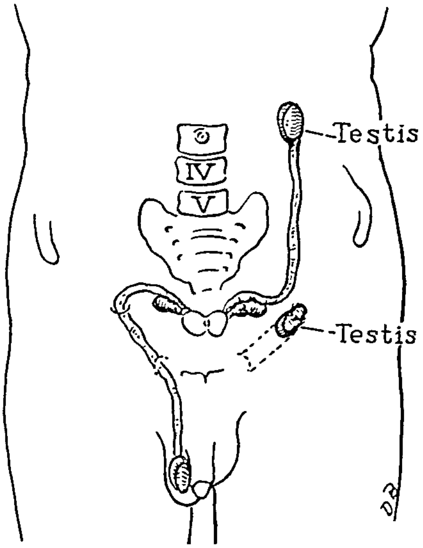

Fig. 2. Artist's conception of operative findings. Coronal view

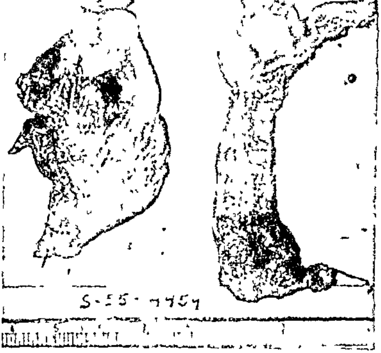

FIG. 3. Gross findings of surgically removed specimen. Upper testis is on right

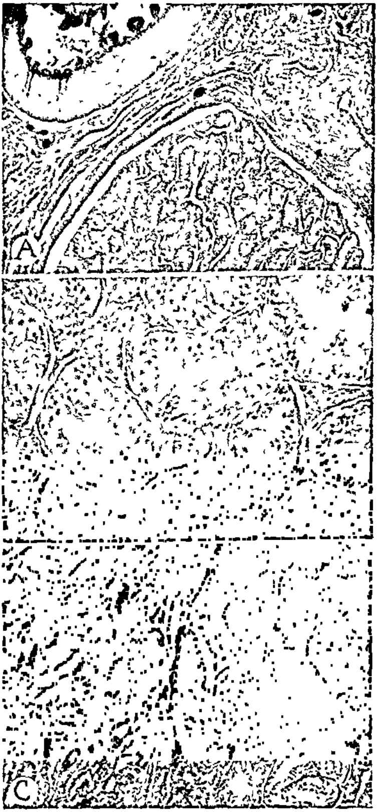

FIG. 4. Photomicrographs. *A*, upper testis showing testicular structure and adjoining vas. *B*, high power view of upper testis to show complete absence of spermatogonia. *C*, lower testis to show similar germinal aplasia of spermatic tubules. Note proliferation of rete tubules on right.

superiorly, and removed from above downward. The usual hernial repair closure terminated the procedure.

The patient was discharged on the eighth hospital day, with the wound edges healing well.

Pathological findings (gross S-55 4454): The findings are reconstructed diagramatically in the accompanying drawings (figs. 1 and 2). The spermatic cord was represented by an elongated structure which had been previously divided. Each cord segment was 8 cm. in length and approximately 1.5 cm. in diameter. In each divided segment a small testis and epididymis were identified (fig. 3). Each testis measured 0.8 cm. in maximal diameter, and on cut section showed yellow parenchyma which strung fairly easily. The lower testis was judged to be just below the internal ring within the inguinal canal. The other testis was located within the abdominal cavity about 9 cm. superior to the lower testis. The superior testis was attached to the vas deferens, and continuity between the two structures could be demonstrated (fig. 4, *A*). The inferior testis showed no connection to the vas as it passed beside the gonad. The entire vas was about 16 cm. in length, and was apparently cut prior to its termination in the seminal vesicle.

Microscopic description: Both testes were similar and showed spermatic tubules lined only by Sertoli cells (fig. 4, *B*). No spermatogonia were visible, germinal aplasia being complete. The lower testis showed a remarkable degree of proliferation of the rete tubules, but no connection to a vas deferens could be established (fig. 4, *C*). Serial sectioning, however, was not done.

Diagnosis: Polyorchidism (double testis on left); cryptorchism, left; germinal aplasia of left testes; duplication of epididymis, left.

SUMMARY

A case of duplication of a left undescended testicle associated with an indirect inguinal hernia is presented.

Both undescended testes were atrophic and revealed germinal aplasia.

The upper testis was located within the abdominal cavity and showed connection with the epididymis and vas deferens.

The lower testis was in the inguinal canal, and had its own epididymis, but connection to the vas could not be demonstrated.

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THE JOURNAL OF UROLOGY
Vol 75 No 5 May 1956
Printed in U S A

BILATERAL ADENOMATOID TUMOR OF EPIDIDYMIS

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Although primary tumors of the epididymis are rare, only 134 cases having been found in the world literature by Longo, McDonald and Thompson,[1] it was noted that the adenomatoid tumor accounted for 53 per cent of the entire group Of all the primary tumors 74 per cent were benign and 26 per cent malignant, a reversal of the ratio of 40 per cent benign to 60 per cent malignant which had been found in a review[2] 15 years earlier This reversal was brought about chiefly by the increase in adenomatoid tumors or mesotheliomas which had been recognized and reported The bilateral occurrence of an adenomatoid tumor of the epididymis led to this review

Wentzell[3] found that 98 of these tumors had been reported and added two more to bring the total to 100 Any accurate compilation is difficult because of the variety of designations appearing in the literature The tumor was first described by Sakaguchi[4] and was called adenomyoma, perhaps still a good term Stout[5] reported on conditions of the epididymis simulating carcinoma and mentioned a fibromyoma which has been regarded by Lee et al [6] as a mesothelioma Eisenstaedt[7] reported a single fibromyoma of the epididymis which Lee did not include in a list of mesotheliomas previously diagnosed otherwise Hinman and Gibson[8] presented an adenocarcinoma or fibroadenoma which might well be placed in this group A tumor reported by Spivack[9] was diagnosed leiomyoma Glandular elements were present but were described as remnants of normal tissue Charache[10] described a benign tumor of the lower pole of the epididymis which he called lymphangioma, now also regarded as mesothelioma[6] as well as instances of mixed leiomyoma and lymphangioma [11] [12] The single specimens

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Accepted for publication December 14 1955

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described by Blumer and Edwards[13] and by Gordon-Taylor and Ommaney-Davis[14] were called adenomas. Sworn, Marshall, and Edwards[15] reported two benign "adenomatous" tumors which they felt were best designated as "mixed tumors."

Since Evans[16, 17] and Mackay[18] used the term mesothelioma, many similar tumors have been reported under this name.[6, 19, 20] The term adenomatoid tumor introduced by Golden and Ash[21] in 1945 seems to have been even more widely used.[1, 3, 22-28] Although descriptions of angiomatoid tumors,[29] hemangiomas and lymphangiomas of the epididymis[30, 31] still appear, many of these tumors may well belong with the adenomatoid group.

The origin of the adenomatoid tumor has not been settled. Falk and Konwaler[25] favored an inflammatory rather than a neoplastic process. Bothe[32] reviewed the theories by origin and noted that a myomatous tumor had been called a "pseudo-tumor" by Oberndorfer who thought this was the result of a chronic inflammatory process. Morehead[28] described "angiomatoid formations" and supported the hypothesis that they are derived from mesenchymal cells. Golden and Ash[21] proposed that the primary unit of the tumor is epithelial. A mesothelial origin has received the greatest support[6, 17, 18, 20, 27, 30] in explaining the pathogenesis of this tumor in the epididymis, testicular tunics, and spermatic cord,

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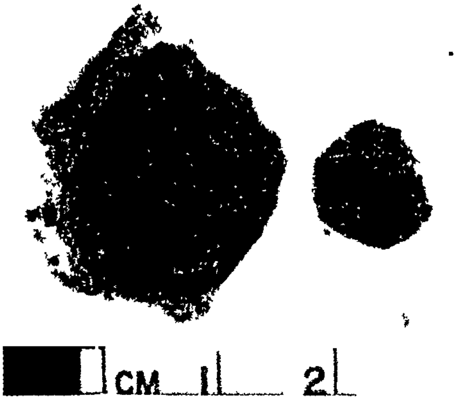

FIG 1 Gross specimens Small tumor, 1 cm in diameter from right epididymis and larger tumor, 2 3 cm in diameter, from left epididymis Both had fibrous capsules

as well as in the female genital tract Gordon-Taylor and Ommaney-Davis,[14] and Codnere and Flynn[12] considered the mesonephrogenic origin most likely In support of the mesonephrogenic origin, Longo[1] noted that this tumor has been found along the course of the mesonephros in both the male and the female He proposed that the adenomatoid tumor be regarded as a hamartoma of the mesonephros

Whatever the histogenesis of this tumor may be, there is no longer any question of its benign nature There is no recurrence after epididymectomy or local excision The tumor is usually small, less than 2 5 cm in diameter in most of the cases which have been described, firm, encapsulated, and more frequently found in the globus minor The age of incidence has been reported from infancy to the seventh decade

In 1939 Milner and Gilbert[33] reported a case of bilateral leiomyoma, the second most common benign tumor of the epididymis There was no mention of any adenomatoid areas Gordon-Taylor and Ommaney-Davis,[14] and Glaser[19] referred to a bilateral leiomyoma reported by Foged in 1939 Lazarus and Friedman[30] mentioned another bilateral leiomyoma reported by Gallizia and Marazzini in 1949 In reference to adenomatoid tumors Longo[1] noted, "No instances of multiple tumors were recorded in this group, nor were there cases of bilateral involvement" Rapoport and Morgan[26] also stated, "Bilaterality has not been reported"

CASE REPORT

A 48-year old white man, the father of five children, was found to have a scrotal mass on a routine physical examination He was referred for urological consultation There were no symptoms referable to the genito urinary system

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
Printed in U.S.A.

ABSORPTION OF IRRIGATING SOLUTION AND ASSOCIATED CHANGES UPON TRANSURETHRAL ELECTRORESECTION OF PROSTATE

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During transurethral electroresection of prostate,† or at the close of such a procedure, the patient may abruptly become hypertensive, restless, nauseated, dyspneic, and cyanotic and complain of blacking out. Our purpose was to find: 1) whether there is correlation between occurrence of hypertension and amount of fluid-gain, and 2) whether some of the absorbed water rapidly becomes intracellular. We also wished to check the presumed diuretic effect of hypertonic sodium chloride given in amount calculated to restore normal concentration of sodium and chloride in the extracellular fluid‡ in spite of the hypervolemia. This is a continuation of previous work on absorption of water and solutes through the bladder and open prostatic fossa (Maluf, '53, '55; Hagstrom, '55).

METHODS

Shortly prior to TEP, blood was drawn for serum sodium, chloride, and protein and for hematocrit. The patient was weighed naked on calibrated bed-scales (fig. 1) immediately before being transferred to the cystoscopy table for the resection. The cerebrospinal fluid§ pressure was measured in the horizontal lateral decubitus with use of a No. 22 spinal needle and without loss of CSF. About four cubic centimeters of the fluid were collected for measurement of chloride and protein concentration. The spinal anesthetic was then introduced through the needle. The volume of fluid which the patient received by intravenous drip between the pre- and postoperative weighings was noted and converted into grams.

The irrigation fluid was 1.2 per cent glycine in sterile water, as prescribed by Nesbit and Glickman who noted that 2.1 per cent glycine is isotonic with plasma but that 1.2 per cent, while hypotonic, is not hemolytic in the test-tube or the body. In most performances the initial hydrostatic pressure of the irrigation fluid was 135 cm.; more fluid was added when the height fell to about 115 cm. In a few cases the hydrostatic pressure ranged between 105 and 85 cm. of water. The volume of fluid ranged between 14 and 52 liters.

Immediately after completion of the operation the pressure of the CSF was again measured and about four cubic centimeters collected for chloride and protein. Blood was drawn for serum sodium, chloride, and protein and for hematocrit and submitted for immediate analysis because we considered the

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Accepted for publication October 24, 1955.

* Present address: 4867 Sunset Blvd., Los Angeles 27, Calif.

† Abbreviated TEP throughout this paper.

‡ Abbreviated ECF throughout this paper.

§ Abbreviated CSF throughout this paper.

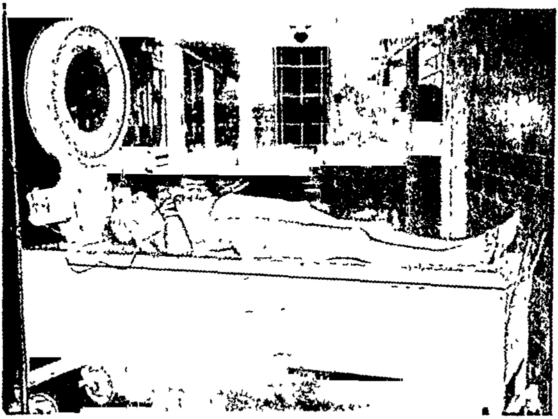

FIG. 1. Weighing of patient on bed-scales "Toledo" scale; from Toledo Scale Company, Toledo, Ohio.

postoperative sodium and chloride levels as crucial for adequate postoperative therapy. The patient was again weighed naked on the bed-scales. The weight of the indwelling catheter and the small quantity of fluid received by intravenous drip was subtracted from this reading. Cognizant of water-absorption during TEP, we maintained intravenous drip during resection only to keep the indwelling needle open. The postoperative fluid intake and output were recorded. The following morning the patient was weighed on the bed-scales for the third time and blood drawn for serum sodium, chloride, and protein and for hematocrit.

RESULTS

1. Controls. The patients who underwent transvesical prostato-adenomectomy (open surgery controls) or transurethral litholapaxy under spinal anesthesia showed no significant change in weight and no change in $[\mathrm{Na}]_s$,* $[\mathrm{Cl}]_s$, or $[\mathrm{Protein}]_s$ in the immediate postoperative period. Their CSF pressure fell slightly or not at all. The $[\mathrm{Cl}]_{CSF}$* and $[\mathrm{Protein}]_{CSF}$ tended to fall slightly. Thus Δ† Cl_{CSF} averaged -6 mEq/liter with σ‡ $= 3.9$ and $[\mathrm{Protein}]_{CSF}$ averaged -3.2 mg. per 100 cc with $\sigma = 1.4$.

2. Changes in patients undergoing TEP. a) Weight. Fourteen of the 15 patients gained weight during the operation. The range of weight-gain was 0.10 kg. to 4.5 kg. (average 1.99 kg.). One of the patients lost 200 gm. of weight, probably consisting largely of blood and a 33.5 gm. adenoma. Two patients gained over 4 kg. in weight during resections lasting 80 minutes each. Blood-loss was moderate in these patients. The surgical capsule in these 2 cases was exposed throughout but weight of adenoma was only 9.5 and 17 gm. Both patients became hypertensive, apprehensive, dyspneic, and restless. One of them subsequently went into shock probably from blood-loss. The other patients showed no such reactions although two of them gained about 3 kg. of fluid (3.0 and 3.5 kg.). It thus appears that an elderly male patient, who is a fair surgical risk and who is about 60 kg. preoperatively and who becomes apprehensive, dyspneic and hypertensive during TEP, has absorbed over 3.5 kg. of irrigation fluid within approximately one and a half hours.

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* Symbols or names of chemical elements or compounds within brackets indicate concentration. Subscript *s* indicates concentration in serum; subscript *CSF* indicates concentration in cerebrospinal fluid.

† Δ symbolizes difference or change

‡ σ is standard deviation from the average.

b) *Serum sodium* showed a decline immediately at the close of resection in all cases except one (fig. 2, patients No. 1 and 8). The average fall was 11.2 mEq/liter. The 2 patients who became hypertensive underwent pronounced drop in $[Na]_s$ of 32 and 14 mEq/liter (table 1, patients No. 1 and 8). A third patient (table 1, patient No. 4), who showed a slight rise in arterial pressure during resection had a drop in $[Na]_s$ of 16 mEq/liter. The only other patient who showed a drop in $[Na]_s$ exceeding 10 mEq/liter had an uneventful operative and postoperative course.

The *actual* immediate postoperative $[Na]_s$ was compared with the $[Na]_s$ which would be expected, i.e., the *theoretical* $[Na]_s$, if the absorbed water remained exclusively within the ECF. The initial ECF content of the body was assumed to be 20 per cent of the initial body weight. Thus,

$$\text{theoretical } [\text{Na}]_S = \text{initial } [\text{Na}]_S \times \frac{\text{ECFW}}{(\text{ECFW} + \text{W})},$$

in which *ECFW* is the calculated initial weight of the extracellular fluid compartment and *W* the weight-gain. For example, initial weight of patient No. 1 was 53.2 kg. His ECF volume or weight would be 20 per cent of that, i.e., 53.2/5 liters or kilograms. His immediate postoperative $[Na]_s$ was 110 mEq/liter and his weight-gain during resection was 4.5 kg. If all the water absorbed remained extracellular, the

$$\textit{theoretical } [\text{Na}]_S = 142 \text{ mEq/liter} \times \frac{10.6 \text{ liters}}{(10.6 \text{ liters} + 4.5 \text{ liters})}$$

$$= 99.7 \text{ mEq/liter, which is } 110 - 99.7 \text{ mEq/liter less than the } \textit{actual } [\text{Na}]_S.$$

Table 1 shows that the actual $[Na]_s$ immediately after transurethral resection is nearly always considerably higher than the theoretical $[Na]_s$ based on the assumption that the water absorbed remains in the ECF. The implication is that some of the water absorbed enters the intracellular compartment. This is corroborated by similar changes in $[Cl]_s$ (below).

During the latter half of the day of surgery and during the first postoperative day the $[Na]_s$ returned to normal (fig. 2). This occurred in most cases by diuresis and is correlated with simultaneous fall in weight during this period. In one instance (patient No. 1) 250 cc of 5 per cent NaCl (≡ 12.5 gm. NaCl) were given intravenously in the immediate postoperative period to raise the $[Na]_s$ and $[Cl]_s$ to normal and thus promote diuresis (see Commentary). The amount

TABLE 1. *Concentration of serum sodium and chloride immediately after resection*
A = actual; T = theoretical. ΔWgt. = change in net weight during resection.

Patient No.	$[Na]_s$			$[Cl]_s$			Weight (% Initial)
	Actual (A)	Theoretical (T)	A − T	Actual (A)	Theoretical (T)	A − T	
1	110	99.7	10.3	68	65.3	2.7	8.45
2	122	113	9.0	80	79.2	0.8	4.68
3	147	137	10.0	96	94	2.0	0.45
4	135	130	5.0	88	79.2	8.8	4.2
5	141	144.5	−3.5	96	98.8	−2.8	−0.21
6	133	135	−2.0	87	91	−4.0	1.1
7	141	138.8	2.2	90	89.4	0.6	1.1
8	126	101	25.0	87	67	20.0	6.88
9	133	111	22	78	68	10.0	5.48
10	134	128	6.0	90	86.2	3.8	2.5
11	133	124	9.0	88	84.3	5.7	1.78
12	139	141.3	−1.3	92	97.6	−5.6	0.11
13	139	114	25	92	73.5	18.5	5.32
14	136	122	14	88	79.5	8.5	2.23
15	130	118	12	90	82	8.0	1.80

given was calculated from the concentration-deficit and the estimated ECF volume (cf. Maluf, '54, p. 1106).

c) Serum chloride behaved similarly to $[Na]_s$ (fig. 2 and table 1). The actual immediate postoperative $[Cl]_s$ was higher than the "theoretical" $[Cl]_s$ calculated from the weight-gain and assuming that all the water absorbed remained in the ECF (table 1). Passage of some of the absorbed water intracellularly is thus inferred. During the latter half of the day of surgery and during the first postoperative day the $[Cl]_s$ returned to normal (fig. 2). This accompanied the course of the $[Na]_s$ (see previous paragraph).

d) Serum protein and the hematocrit tended to fall during resection (fig. 2). This roughly correlated with extent of blood-loss and with amount of fluid absorbed. Blood-loss was not measured in this study and therefore a differential cannot be made.

e) Concentration of chloride in the CSF typically fell during resection. The drop averaged 3.7 mEq/liter (σ = 4.28). This drop may not be significant as it is within range of the controls (above).

f) Concentration of protein in the CSF deviated slightly in both directions during resection. The changes averaged zero.

g) Pressure of CSF tended to rise during resection. The change averaged +79 mm. CSF. By far the greatest rise (+198 mm. CSF) was in patient No. 1, who showed the greatest gain in weight and who became hypertensive.

h) Effect of hydrostatic pressure of the irrigation fluid is doubtless significant. All resections except two were performed with irrigation pressures of 115 to 135 cm. of water. The remaining two (patients No. 12 and 15) were operated on with pressures of 85 to 105 cm. of water. These two gained 0.1 and 1.1 kg. of fluid, respectively, which values are among those of lower magnitude.

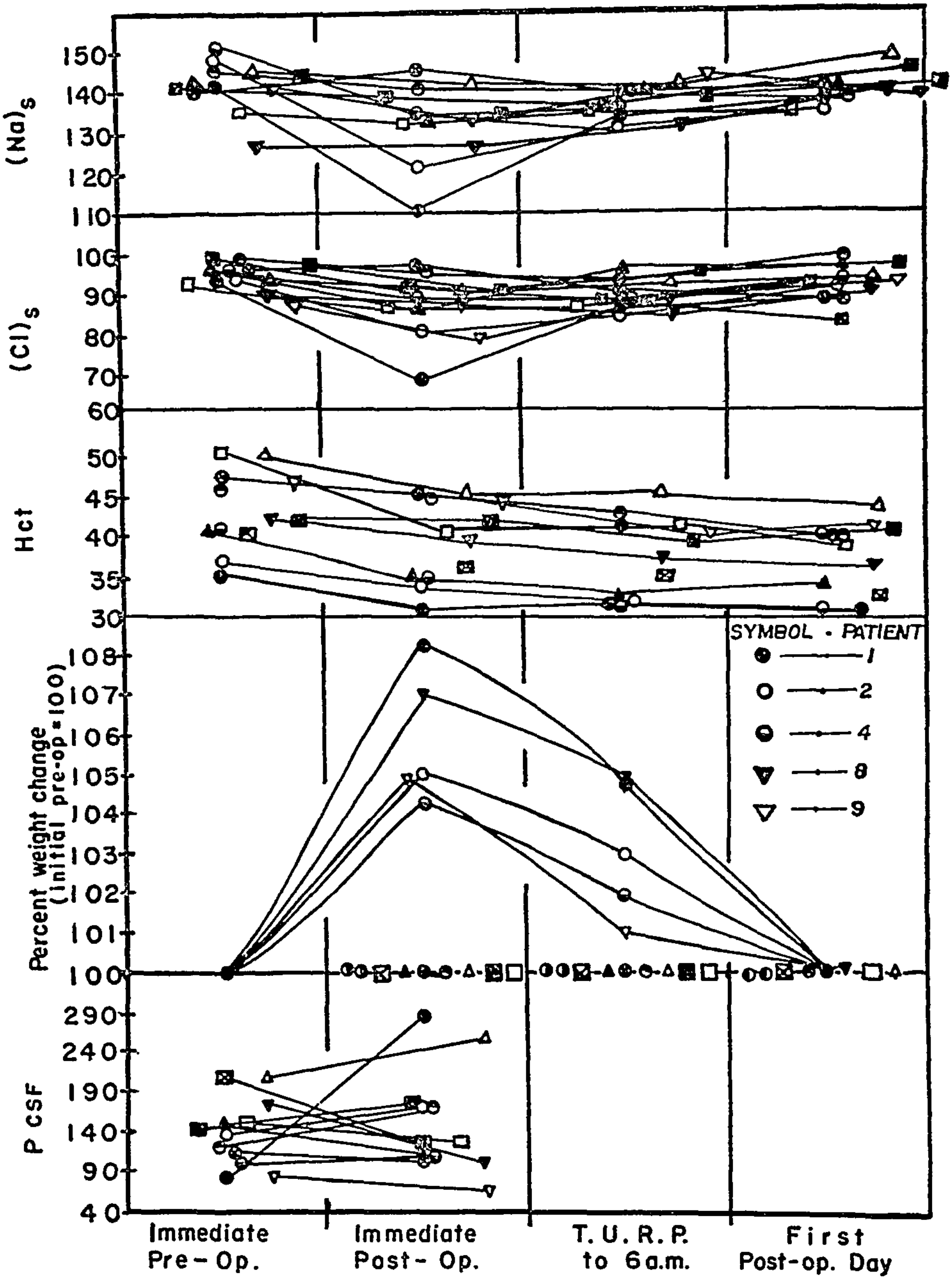

FIG. 2. Graphs depicting changes occurring during transurethral resection of prostate and their postoperative reversal. Each curve represents a single patient. Symbol of patient's number is indexed on right of weight curves. Concentrations of serum sodium, $[Na]_s$, and serum chloride, $[Cl]_s$, are in mEq/liter. The hematocrit, Hct, is in gm./100 ml. Weight is expressed as "per cent weight change" (patient's initial preoperative = 100). Cerebrospinal fluid pressure, P_{CSF}, is in mm. of CSF.

COMMENTARY

1) Absorption of irrigation fluid. If the irrigation fluid is to maintain visibility its hydrostatic pressure must not only exceed venous pressure, which is only a few centimeters of water, but should be high enough to maintain sufficient velocity through the resectoscope to flush away blood and resected slivers. A pressure much less than 100 cm. of water, i.e., about ten times the venous pressure, is usually not practicable with a nonhemolytic solution. This is the hydrostatic pressure usually employed in Nesbit's department (Lapides). Thus pressure of irrigation fluid (85 to 135 cm. of water in our work) tends to exceed even diastolic arterial pressure although not systolic pressure. The large difference in pressure between irrigation fluid and open intraprostatic veins causes absorption of fluid. Apparently first evidence that irrigation fluid is driven into the circulatory system during TEP was published by Creevy, who noted extraordinary hyperglycemia when 4 per cent glucose was used for irrigation, and by Landsteiner and Finch, who used 0.1 per cent sodium salicylate for irrigation in a few patients. Maluf ('53, '54) showed that the normal bladder is impervious to glucose. The inference is that glucose passed through the open prostatic veins at the end of a complete transurethral prostato-adenomectomy. The large amount of fluid—as much as 4.5 liters—which can be driven into elderly men within an hour or so is revealed in the present work.

2) Effects of type of irrigation fluid. Irrigation fluids suitable for resection may be classified into three main types and the effects they tend to have on the body fluids graded 0 to 4+:

a) *Hypotonic, hemolytic, practically nonconductive* (plain water).
  Hypervolemia 2+; possible rapid diffusion intracellularly.
  Hypotonicity 4+; hemolysis and water-intoxication with possible cerebral edema.
  Hypoelectrolytemia 4+.
b) *Hypotonic, nonhemolytic, practically nonconductive* (1.2 per cent glycine).
  Hypervolemia 3+.
  Hypotonicity 2+; not hypotonic enough to be hemolytic but may result in water-intoxication with possible cerebral edema.
  Hypoelectrolytemia 4+.
c) *Isotonic, nonhemolytic, practically nonconductive* (2.5 per cent glycine).
  Hypervolemia 4+.
  Hypotonicity 0; hemolysis and cerebral edema excluded.
  Hypoelectrolytemia 4+.

a) *Plain water.* When signs of hypervolemia occur with plain water they are especially ominous because they indicate that a large amount of the hemolytic liquid has been absorbed and that tendency to oliguria from marked hypoelectrolytemia (see below) is added to tendency to oliguria from massive hemoglobinemia. Upon watching a resection some years ago we became impressed with the operator's remark that "whenever a patient becomes hypertensive during my resection he becomes oliguric; this patient has become hypertensive . . . he will be oliguric." That patient died from uremia after 2 weeks without having excreted appreciable urine and in spite of expert attempts at maintenance of a normal water and electrolyte state. Plain sterile water was used for the irrigation. It was the opinion that perforation of the capsule tends to result in hypertension; a vague nervous reflex was postulated. The present work indicates that onset of hypertension during or shortly after TEP may be due to overhydration. When this occurs by massive entry of plain water, dangerous hemolysis can result (Creevy '47, '48, Creevy and Webb, Landsteiner and Finch, McLaughlin et al., Biorn and Greene, Woodruff and Firminger, Robbins et al., Goodwin et al., Bulkley et al.).

b) One and two-tenths per cent glycine. Use of relatively nonconductive, slowly diffusible, nonhemolytic solutes, such as glucose (Creevy), glucose-insulin (Dees et al.), mannitol (Goodwin et al.), or glycine (Nesbit and Glickman, Garske et al., Robbins et al.) in the irrigating water has eliminated renal shutdown from hemolysis. One and two-tenths per cent glycine, which we have used in this series, is hypotonic although not enough so to become hemolytic (Nesbit and Glickman). Complications which may arise from copious absorption of 1.2 per cent glycine can thus be due to hypervolemia as such, to hypoelectrolytemia and, perhaps, to hypotonicity with exclusion of hemolysis. It is conceivable and not disproven that excessive absorption of hypotonic, 1.2 per cent glycine may lead to water-intoxication and cerebral edema. Hypertension which is associated with absorption of a few liters of 1.2 per cent glycine may be due to expansion of the ECF volume, specifically of the cardiovascular volume, and/or to passage of some of the absorbed water intracellularly, specifically into brain-cells producing cerebral edema. We have shown above that intracellular diffusion occurs. Marked rise in CSF pressure, exclusively in the patient who became hypertensive with absorption of 4.5 liters of water (fig. 2, patient No. 1), may be taken to indicate that cerebral edema was a contributing factor in the production of the hypertension. Against this hypothesis is: i) occurrence of hypertensive syndrome even when 2.5 per cent glycine had been used (see below); ii) fall in $[Cl]_{CSF}$ and $[Protein]_{CSF}$ is insignificant during TEP (see Results); iii) Na^+ and Cl^- are readily diffusible from the brain (Yannet); the brain-cells, in presence of mild to moderate hypotonicity may thus lose electrolyte more readily than absorb water; and iv) the CSF pressure can be raised by giving even isotonic NaCl or dextrose solution intravenously (Weed and McKibben, Fishman).

c) Two and five-tenths per cent glycine. Hypertension occurring during or at the close of TEP with the nearly isotonic 2.5 per cent glycine may be construed to be due to hypervolemia as such. Typical hypertensive reactions (see below) have occurred as frequently in our hands with 2.5 per cent glycine as with 1.2 per cent. Hypertension in these cases too was not preceded by drugs. Thus, hypervolemia, as such, can elicit the syndrome of hypertension.

Because the irrigating fluid, of necessity, is practically free from electrolyte, all suitable solutions will produce hypoelectrolytemia, including hyponatremia and hypochloremia, when absorbed. The degree of fall of $[Na]_s$ and $[Cl]_s$ during resection rather closely parallels the gain in weight, i.e., gain in fluid (table 1 and fig. 2). Disturbances produced by hypervolemic hypoelectrolytemia are treated below.

3) Syndrome of hypertension. Arterial pressure may rise during TEP even when no drug has been given. Typically this is accompanied by restlessness, nausea, vomiting, dyspnea, cyanosis, disorientation, semicoma, and excessive welling of blood through the open prostatic veins. Arterial bleeding from the resected site may recur or increase. Atelectasis, pneumonitis, or pulmonary abscesses may result if vomitus is not immediately aspirated. Wardill reports a patient whose aortic aneurysm burst during rising arterial pressure during TEP. Our work indicates that the syndrome of hypertension is the result of hypervolemia, as such, when the amount of fluid absorbed has been excessive, i.e., about 4 liters in 80 minutes. From concentration of salicylate in blood and irrigation fluid, Landsteiner and Finch estimated absorption of one liter. Such a value is rough because of unknown amount of salicylate metabolized by liver and excreted by kidneys. Net change in weight of a patient is the most accurate and easiest way to measure amount of fluid absorbed. Thus the fluid absorbed, during practically complete resection of prostatic adenomas weighing 5 to 32 gm., varied between 100 and 1,250 gm. (Hagstrom). None of Hagstrom's weighed cases, however, became hypertensive. In our present series only 2 patients (Nos. 1 and 8) became hypertensive; these gained 4.5 and 4.1 kg. of fluid within 80 minutes. They had small adenomas and bleeding was moderate. Patient No. 13, who absorbed only 3.5 kg., did not become hypertensive. From study of over 35 weighed cases, we consider that a patient tends to become hypertensive when he absorbs over 6.5 per cent of his initial body weight (table 1). Drop in $[\text{Na}]_s$ or $[\text{Cl}]_s$ is typically proportional to gain in weight. A fall of 20 to 30 mEq/liter is ominous because it indicates absorption of a large amount of fluid.

Effects of massive intravenous infusions have been studied experimentally. Cutting et al. had slight to moderate initial rise in arterial pressure in anesthetized cats. They found that the brain was the one organ of the body which did not gain water after massive infusion with 1 per cent NaCl or isotonic glucose. The animals underwent watery vomiting and diarrhea and showed considerable amount of free fluid in the abdominal cavity, edematous thickening of the stomach, colon, and urinary bladder, gelatinous edema of pancreas, the space between the leaves of the mesentery and the retroperitoneal space, and edema of the lungs and salivary glands. Warthen found definite rise in arterial pressure of dogs at onset of massive intravenous infusions but this was usually followed by a fall. He noted edema of the wall of the stomach and gut, with fluid in gut and peritoneal cavity. Grollman found an insignificant change in arterial pressure during marked expansion of the ECF by 5 per cent glucose in water or plasma electrolyte. Rise in arterial pressure occurred in nephrectomized dogs which had been depleted of ECF. With an overexpanded ECF or cardiac damage, infusion of fluid produced decline in arterial pressure. Rise in CSF pressure upon intravenous administration of isotonic solutions has been noted above.

It is well to weigh patients before and immediately after TEP and to obtain immediate postoperative $[\text{Na}]_s$ and $[\text{Cl}]_s$. This applies especially to the poor risk in whom accurate interpretation of complications is mandatory. Thus, large absorption of fluid may be completely masked by: i) initial low blood-volume and resulting shock from average bleeding; ii) moderate to heavy bleeding; iii) cardiac arrhythmia; iv) myocardial infarction; v) rupture of aneurysm;

and vi) cerebrovascular accident. Contrariwise, excessive loss of blood may be masked by hypervolemia. Onset of hypertension during or at close of TEP may be due to hypervolemia, water-intoxication and cerebral edema (especially if plain water had been used), cerebrovascular accident, or drugs.

4) *Water-intoxication* implies effects of excessive absorption of hypoelectrolytemic solution or of plain water.

a) *Hypervolemia* and resultant hypertension have been discussed. The syndrome of hypertension typically comes to the fore when hypoelectrolytemia is secondary to massive absorption by isotonic or moderately hypotonic glycine, mannitol, or glucose solution, in which cerebral edema and hemolysis probably would not be factors.

b) *Hemolysis* would result from plain water or very hypotonic solutions of the above compounds. This is no longer a factor with our solutions.

c) *Cerebral edema.* Equilibrium of water is established rapidly between brain, spinal cord and blood (Lavietes et al., Bering). Weed and McKibben noted that giving plain water intravenously to etherized cats caused marked sustained rise in CSF pressure which was much higher and more sustained than with identical quantity of Ringer's solution. Plain water produced marked swelling of the brain as noted at trephine holes. Ferraro noted gross and microscopical evidence of cerebral edema in rabbits given plain water intravenously. Unfortunately there is no hint of how much was required to produce these changes. Weir et al., Misawa, and Rowntree noted neurotoxic signs (ataxia, twitching, slow shallow breathing, drowsiness, convulsions) in hypervolemic hypoelectrolytemic animals. Headache, nausea, asthenia, incoordination, and staggering gait occurred in patients with diabetes insipidus who received posterior pituitary extract subcutaneously and their usual 8 to 10 liters of water daily. Miller and Williams found that giving large amounts of fluid (2.5 liters orally in 2 hours) to patients with hypertension and nephritis may cause marked rise in arterial pressure, with headache, dizziness, nausea, dyspnea, and cramps in legs, depending inversely upon the promptness with which the kidneys excreted water. Amberg and Austin drank 3 liters of water in 20 minutes and developed tremors and muscular twitching. Stewart and Rourke noted a near-death from water-intoxication in a young woman who had received about 7 liters of 5 per cent dextrose in water in 36 hours. She recovered spontaneously. Helwig et al. reported death from water-intoxication (vomiting, perspiration, tremors, stupor, convulsions, dilatation of pupils, opisthotonus, and death) of a woman who had been given several liters of tap-water by proctoclysis. The brain showed swelling and cellular vacuolation. They were able to reproduce the phenomenon in rabbits.

d) *Hypoelectrolytemia and renal failure.* A small to moderate fall in $[\mathrm{Na}]_s$ or $[\mathrm{Cl}]_s$ is an adequate stimulus to diuresis by suppressing release of pituitary antidiuretic hormone (Priestley; Haldane and Priestley; Verney; Smirk). A marked fall in $[\mathrm{Na}]_s$ or $[\mathrm{Cl}]_s$, however, seems to inhibit diuresis; this is true not only with normal kidneys and a contracted ECF (McCance; McCance and Widdowson) but also with chronic renal failure and hypervolemia (Schroeder; Bull) or normovolemia (Nickel et al.). The cause for this oliguria in the face of hypervolemia is unknown; it may be a distorted attempt by the kidney to conserve Na, which is low in concentration but normal in absolute quantity. Increase in intracranial pressure as such does not appear to affect renal function (Fishman and Halla).

e) Hypoelectrolytemia and shock. It was pointed out above that the syndrome of hypertension from hypervolemia may be masked by blood-loss and shock, in spite of expansion of the ECF, because of contraction of the vascular volume. It is pertinent to inquire, however, whether hypotonicity or hypoelectrolytemia, as such, may produce shock in presence of normal total electrolyte content. Danowski et al. and Elkinton et al. ('46, '47) produced nephrectomized dogs with a hypotonic but expanded extracellular volume and which thus corresponded to patients undergoing TEP. The cardiac output, circulation-time, and arterial pressure were either unaffected or improved. On the other hand, restoring concentration alone, as with 5 per cent dextrose in water, in salt-depleted animals, failed to relieve the circulatory collapse. When both volume and concentration were restored by saline infusion, prompt recovery from shock occurred. In transposing these findings to the clinic, it appears that patients who had been depleted of salt preoperatively, as by low-salt diet, mercurials, acute relief of chronic lower urinary tract obstruction (Wilson et al.), and by kidneys capable of only isosthenuric urine (Sawyer and Solez; White and Rubin) are not likely to improve by absorption of electrolyte-free irrigation fluid.

5) Factors determining volume of fluid absorbed. The amount of fluid absorbed will depend upon at least three variables: i) hydrostatic pressure of irrigating fluid, ii) degree of completeness of resection, i.e., exposure of intraprostatic venous channels; and iii) time of exposure. The third factor is not exactly the resection-time because a slow resection well within the limits of the adenoma may produce little or no absorption (Biorn and Greene; Robbins et al.; Nicolai and Cordonnier; Hagstrom; Lapides). Robbins et al. and Nicolai and Cordonnier continue to use plain water and have no noticeable morbidity from this because they follow two rules: i) use of low hydrostatic pressure (about 60 cm.), which is easier with a hemolytic solution; and ii) avoiding resection beyond adenoma. Lapides uses about 100 cm. of pressure and 1.2 per cent glycine. He finds no appreciable water-absorption as indicated by absence of drop of $[\mathrm{Na}]_s$ and $[\mathrm{Cl}]_s$ (Murphy, Iob, and Lapides). It appears that if one uses plain water one can get by without appreciable absorption if one works under low hydrostatic pressure. A nonhemolytic solution necessitates a higher irrigation pressure and, other things being equal, augments danger of over-hydration although it eliminates hazard of renal shut-down from hemolysis.

6) Value of hypertonic sodium chloride. We have noted above that marked hypoelectrolytemia may produce oliguria in spite of hypervolemia. "The predicament of hypotonicity in the presence of anuria can be solved only by providing an hypertonic solution of electrolyte" (Gamble, '49). Chabanier and Lobo-Onell and Schlegel et al. noted that small volumes of concentrated NaCl are beneficial in restoring the excretory activity of the kidneys. Darrow reversed the downhill course of a boy in water-intoxication with convulsions by administering hypertonic NaCl and $NaHCO_3$ intravenously. Isotonic solutions had no effect. Rowntree caused immediate recovery from convulsions in patients and animals with water-intoxication by giving 10 per cent NaCl intravenously. We have used hypertonic (5 per cent) NaCl only in the patients who became markedly overhydrated with sharp drops in the $[Na]_s$ and $[Cl]_s$ in the immediate postoperative period. The amount of NaCl given was calculated from the concentration-deficit. The symptomatic response as well as the diuresis and loss of excess fluid were dramatic. Weed and McKibben and Sachs et al. noted shrinkage in brain-volume and fall in CSF pressure upon administration of hypertonic NaCl intravenously to animals. This has been corroborated by Wilson et al. and a host of others. Wilson et al. found that intravenous administration of hypertonic glucose, on the other hand, results in fall in CSF pressure followed by a marked rise. Since the concentration-gradient of glucose across the cell-membrane soon disappears, movement of water back into the cell occurs, the brain-volume increases and intracranial pressure rises. These findings have been affirmed by Fishman who also indicated that Na penetrates into the CSF relatively slowly.

SUMMARY

Fifteen consecutive patients undergoing TEP were studied for weight-change and for change in $[Na]_s$, $[Cl]_s$, and $[Protein]_s$ during the operation. Changes in CSF pressure and in $[Cl]_{CSF}$ and $[Protein]_{CSF}$ were recorded. The irrigation fluid was 1.2 per cent glycine.

Control patients who underwent transvesical prostato-adenomectomy or transurethral litholapaxy under spinal anesthesia showed no significant change in weight, nor in $[Na]_s$, $[Cl]_s$, or $[Protein]_s$ in the immediate postoperative period. Their CSF pressure fell slightly or not at all.

Fourteen of the 15 patients gained weight during TEP. Two patients gained over 4 kg. during the resection period of 80 minutes and developed the syndrome of hypertension. It appears that a patient who is a fair surgical risk, who is about 60 kg. preoperatively, and who becomes apprehensive, dyspneic, and hypertensive during TEP, has absorbed over 3.5 kg. of irrigation fluid within approximately one and a half hours.

$[Na]_s$ fell at close of resection in all cases except one. The two patients who exhibited hypertensive reactions underwent pronounced drop in $[Na]_s$. The actual $[Na]_s$ immediately after TEP is nearly always considerably higher than the theoretical $[Na]_s$ based on assumption that water absorbed remains in the ECF. The inference is that some of the water absorbed becomes intracellular. This is corroborated by identical changes in $[Cl]_s$.

During the latter half of the day of surgery and during the first postoperative day the $[Na]_s$ returned to normal. This occurred in most cases by diuresis and was correlated with simultaneous fall in weight.

Concentrated (5 per cent) NaCl has been used effectively to promote diuresis and relieve symptoms of hypoelectrolytemic hypervolemia. The amount given is calculated from the deficit of $[Na]_s$ and $[Cl]_s$.

[Cl]$_{CSF}$ typically fell during the TEP The drop, however, was within range of the controls and is thus probably insignificant

[Protein]$_{CSF}$ did not alter significantly

Pressure of the CSF tended to rise during TEP. The change averaged +79 mm CSF By far the greatest rise was in the patient who underwent greatest gain in weight

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
Printed in U.S.A.

PRESENT STATUS OF TREATMENT OF CARCINOMA OF PROSTATE WITH RADIOACTIVE MATERIALS

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During the past 2½ years, we have had the opportunity of using radioactive gold (Au^{198}), chromic phosphate (P^{32}), and yttrium chloride (Yt^{90}) in the treatment of patients with carcinoma of the prostate gland (table 1). Although sufficient time has not elapsed to fully evaluate any of these materials, we feel that it is worthwhile to bring our results up to date and to get some indication as to how effective interstitial irradiation has been in treating these carcinomas. On the basis of previous animal experiments, we have shown that radioactive gold, phosphorus and yttrium are all apparently safe to use without danger to distant organs, and that all three materials are capable of destroying normal and carcinomatous prostatic tissue as well as some regional lymphatic tissue.[1, 2, 3] We have further shown that destruction of tissue with any of these materials depends chiefly upon uniform distribution of the radioactive colloid throughout the prostate gland or tumor mass. This is due chiefly to the fact that the effective range of tissue destruction by the beta rays is only a few millimeters, making it necessary to have very complete distribution in order that the radiation will be sufficient to destroy all the tumor in a given area. Our animal studies indicated that by the ordinary methods of injection, using multiple needles suprapubically with a ratchet type, pressure syringe, and the addition of the spreading agent hyaluronidase, distribution was very patchy. Large areas were apt to be unaffected and at times normal prostate persisted within a large area of radiation scar.

With this background of experimental work, we approached the clinical use of radioactive materials quite critically and cautiously. Patients were chosen for injection carefully and all cases are being followed. The majority of patients were treated at Chicago Wesley Memorial Hospital, and the rest at the Veterans Administration Research Hospital where more detailed studies and followup were often possible. In addition to the ordinary laboratory studies routinely carried out at Wesley Hospital, it was possible at the Veterans Hospital for the Radio-Isotope Laboratory to study urinary excretion of radioactive substance daily for the first 5 days following injection. Blood samples were also drawn at 1-

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Read at annual meeting, North Central Section of American Urological Association, Chicago, Ill. September 29–October 1, 1955.

* Markle Scholar in Medical Science.

[1] Cooper, J. A. D., Bulkley, G. J. and O'Conor, V. J.: Intraprostatic injection of radioactive colloids. I. Distribution and excretion following injection of radioactive colloids in the dog. J. Urol., 71: 624–627, 1954.

[2] Bulkley, G. J., Cooper, J. A. D. and O'Conor, V. J.: Intraprostatic injection of radioactive colloids. II. Distribution within the prostate and tissue changes following injection in the dog. Trans. Am. Ass. Genito-Urin. Surg., 45: 57–65, 1953.

[3] Bulkley, G. J., Cooper, J. A. D. and O'Conor, V. J.: Intraprostatic injection of radioactive yttrium chloride in the dog. Surg., Gynec. & Obst., 100: 405–408, 1955.

TABLE 1

Isotope	Form	*Half Life* (Days)	E B* Mev.	Max. Range	ER/mc/g†
Au^{198}	Colloidal gold: d = 0.2 microns	2.7	0.32	8.0	82‡
P^{32}	Chromic phosphate: d = 2–4 microns	14.5	0.695	3.8	885
Yt^{90}	Yttrium chloride	2.6	0.90	11.0	200

* Average energy of beta particles.

† Equivalent roentgen delivered for complete decay of 1 mc./gm. tissue.

‡ Beta + gamma radiation assuming .6 r/gram for gamma radiation.

minute intervals for the first 10 minutes following injection, and regularly thereafter for 8 hours to determine blood levels of the isotope. Liver function tests were done preoperatively. All of these Veterans Hospital patients are being brought back at 3-month intervals for repeat perineal punch biopsy, liver function studies, blood counts and skeletal survey. Although these more accurate studies have not been in progress for sufficient time at present, we believe that they will give us a clearer picture as to the effectiveness of isotope therapy as well as a careful check on possible late complications.

MATERIAL AND METHODS

During the period between April 1953 through August 1955, we have treated a total of 44 patients with carcinoma of the prostate, utilizing radioactive gold, chromic phosphate and yttrium (table 2).

Patients with carcinoma of the prostate diagnosed by rectal palpation, perineal Silverman needle biopsy, and/or transurethral resection of tissue were selected for interstitial irradiation with isotopes on the basis of the size of the local growth and the amount of bladder neck obstruction. Those patients having local extension of the carcinoma into the seminal vesicles, periprostatic tissue and lymph nodes, without demonstrable metastases to bone or distant organs were considered to be most favorable subjects for injection. However, some patients with bony and other distant metastases were injected in the hope of causing local shrinkage of the tumor mass, preventing rapid regrowth of obstructing tissue, and preventing recurrent sloughing and bleeding. This latter group of patients had a bilateral orchiectomy done at the time of injection of the radioisotope to give them the maximum possible therapeutic response. The orchiectomy, unfortunately, made evaluation of response to the radiation impossible, except in cases later examined at autopsy. All of the Chicago Wesley Memorial Hospital

TABLE 2

Material	Prostate	Bladder	Urethra
Gold (Au^{198})	34	20	2
Phosphorus (P^{32})	5	—	—
Yttrium (Yt^{90})	5	—	—

TABLE 3. *Gold (Au^{198}) prostatic injection, 34 patients*

9—Died of disease
Temporary benefit from injection—7

10—Living with extensive carcinoma
No apparent benefit

15—Living with clinical improvement
Orchiectomy at time of injection—7

patients have been maintained on oral estrogens. One-half of our Veterans Hospital cases have been treated without the use of estrogens or orchiectomy in order to more accurately evaluate the response to isotope therapy.

Our first three patients were injected by the suprapubic and retropubic route as described by Flocks.[4] All of the others have been injected perineally, using multiple needles introduced into the perineum and guided to the various portions of the tumor mass by a finger in the rectum. We have preferred the latter method because of its simplicity, the short hospital stay, low morbidity, and because we believe that distribution of the radioactive material by this method is comparable to that obtained by the retropubic route. The size of the gland was estimated and a dosage of about 2 mc. per gram in the case of gold and about 1 mc. per gram in the case of phosphorus and yttrium was used. Prior to injection, a catheter was introduced into the bladder and left indwelling in order to collect the radioactive urine. This catheter was left in place until significant radioactivity was no longer present in the urine—usually 48–72 hours. At times a preliminary transurethral resection of the bladder neck was done in order to reduce the mass of tumor and to insure that the patient would be able to urinate postoperatively. The average hospital stay of patients injected perineally was four to seven days.

Blood samples were obtained by venipuncture during the period of injection of the radioactive material and at varying intervals afterwards. Twenty-four hour urine collections were made for 5 days. The radioactive content of the samples was measured in a well counter in the case of radiogold and with a G. Mueller counter for radiophosphorus and radioyttrium.

Thirty-four patients were injected with radioactive gold, utilizing dosages of 45 to 180 mc (table 3). Nine have died of their disease and autopsies were obtained on seven of these. Autopsy studies indicated that local radiation effect, consisting of fibrosis and shrinkage of the primary tumor mass was present to some degree in six of these. No demonstrable radiation damage could be detected in the regional lymphatic tissue. Of the two other patients succumbing to carcinoma, one seemed to obtain subjective and objective improvement for a time following injection, so that there was improvement of obstructive symptoms as well as softening of the gland rectally. Thus, we believe that seven of these 9 patients obtained some temporary and palliative benefit from the radioactive gold injection.

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[4] Flocks, R. H., Kerr, H. D., Elkins, H. B. and Culp, D. A.: Treatment of carcinoma of the prostate by interstitial irradiation with radioactive gold (Au^{198}): A preliminary report. J. Urol., 68: 510–522, 1952.

Ten patients are living following injection of radioactive gold and have extensive carcinoma locally as well as in distant organs. The local mass failed to show much change rectally, and no subjective improvement was noted. These cases all received doses equivalent to the others in the series, yet failed to show much response. Five of these patients have had post-injection biopsies, all of which still showed active adenocarcinoma of the prostate.

Fifteen patients are living and doing well following radioactive gold injection. Four of these patients have had two injections of the material because of recurrent tumor palpable rectally. Six patients have been followed over two years, six over one year, and the rest less than one year. One patient had a negative needle biopsy three months following injection; another had a positive biopsy but has obtained considerable local softening and shrinkage of the prostate. Biopsy material is not available in the remainder of this group. Seven patients in this series had bilateral orchiectomy performed at the same time as the isotope injection so that it would be impossible to say whether the clinical improvement was due to radiation effect or to hormonal effect. These seven patients all manifested distant metastases to bone and we did not feel justified in withholding from them the possible benefit of orchiectomy.

Five patients have had intraprostatic injection of radioactive chromic phosphate by the perineal method (table 4). All of these have been done within the past year, and one was injected twice. Doses ranged between 21.5 and 39 mc. Two patients in this series have had post-injection biopsies, both of which showed active adenocarcinoma. All 5 patients have shown little response symptomatically. Rectally, the prostate has remained hard, nodular and fixed with little of the softening and shrinking often found after gold injection.

Five patients have had intraprostatic injection of radioactive yttrium chloride by the perineal method (table 5). Dosage ranged between 19.5 and 39 mc. One patient died of extensive carcinomatosis ten days following injection, and cannot be truly evaluated. The injection did not seem to have any relation to his death. Two patients in this group are living without subjective or objective improvement. Two patients have obtained clinical improvement and are well with find-

TABLE 4. *Phosphorus (P^{32}) prostatic injection, 5 patients*

2—Living—post-injection biopsy positive
Rectally still hard and nodular

3—Living—rectal findings little changed

TABLE 5. *Yttrium (Yt^{90}) prostatic injection, 5 patients*

1—died of disease—no benefit
2—living with little change rectally
2—living—gland softer and smaller

ings of rectal softening and shrinking of the prostate. One of these patients has a negative biopsy 4 months following injection.

RESULTS

The results of studies on the urine and blood of the patients are shown in table 6. The urinary excretion is highly variable, but occurs in greater part during the first 24 hours following injection. This is in agreement with the results previously reported in animal studies. The radioisotope apparently enters the bladder and urethra at the time of injection.

The highest concentration of radioisotope in the blood was found during the injection period, but fell rapidly during the immediate postoperative period (fig. 1). The peak concentration reached a few per cent of the injected dose per liter of blood. The values for the maximum blood content given in the table were calculated from the concentration and an assumed blood volume of 7 liters. The values represent the upper limit of the circulating radioactive material since complete mixing with the vascular compartment is assumed. The actual content in the entire vascular compartment probably does not reach these values, but, because of the rapid removal of these materials from the blood by the reticuloendothelial systems in the liver, spleen, lung and bone marrow, a more exact figure cannot be determined for the human.

We have been fortunate in the general lack of complications encountered (table 7). Only one serious complication has occurred in a patient who had

Table 6

Patient	% Administered Dose Excreted in Urine			Max. Circulating Blood Content, % Dose
	1st day	2nd day	3rd day	
		Au^{198}		
R. J.	.06	2.50	0.05	
C. H.	38.49	0.10	0.03	
F. Z.	35.90	.17	.07	
C. R.	37.87	1.19	1.36	9.7
C. G.	11.33	0.60	.030	11.3
C. H.	14.40	0.17	0.06	
		P^{32}		
J. K.	1.54	1.42	1.03	
A. E.	.13	.05	.06	
W. B.	0.42	0.04	.06	
W. S.	0.25	9.95		28.7
W. S.	17.55	0.40	0.45	17.1
		Yt^{90}		
W. E.	6.34	1.97	0.48	
W. S.	4.34	0.11	0.47	29.1
L. J.	12.94	0.13	0.23	20.9
C.	23.83	0.51	0.38	

perineal injection of 145 mc. of gold. Within a few days he experienced severe suprapubic pain which persisted for several months. This was accompanied by suprapubic swelling, redness and local pain on pressure. For almost six months he experienced frequent erections to the point of priapism, pain over the pubis and at the base of the penis. Ten months following injection there was residual thickening of the corpora at the base of the penis and occasional pain on urination. We have interpreted these symptoms and findings as being due to extravasation of the gold solution outside the prostatic capsule into the retropubic space and around the root of the penis. Although he has shown good results in local shrinkage and softening of the prostate, this complication has been disabling for a time and has caused the patient considerable distress.

Two patients have experienced transient rectal irritation following radioactive gold injection. This consisted of rectal bleeding for a few days and some irritability of the rectum with frequent stools. These symptoms subsided within a

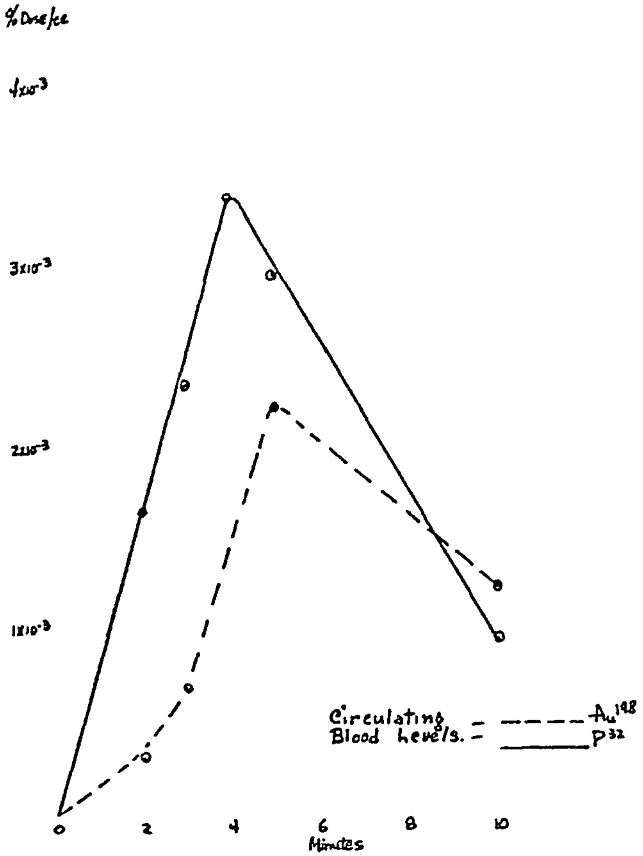

FIG. 1. Radioactive materials in carcinoma of prostate

TABLE 7. *Complications*

1—Retropubic irradiation reaction
2—Temporary rectal irritation
2—Thrombocytopenia; suppression of bone marrow (P^{32})

few days in both instances, and there were no permanent or serious rectal complications. We have carefully avoided the rectum during the perineal injection and believe that the rectal finger makes it possible to avoid complications of this sort more readily than when injection is carried out through the retropubic approach.

Two patients, each of whom had perineal injection of 33 mc. of radio-phosphorus, recently returned to the hospital about one month following treatment complaining of multiple petechiae and ecchymoses over the entire body, including the buccal mucosa. Workup so far has disclosed a thrombocytopenia and suppression of bone marrow in both cases which may be due to radiation, although we have not yet completed the hematologic studies.

DISCUSSION

Our experience to date with the use of radioactive gold in the treatment of prostatic carcinoma has led us to be somewhat less enthusiastic and optimistic than other authors.[4, 5] Careful study of the course of the disease in the patients reported above has shown that clinically about one-half of these have been benefited by interstitial irradiation with gold. Benefit objectively has consisted of shrinkage and softening of the prostate as palpated rectally. In some instances, this has been dramatic to the point of almost "normal" rectal findings, which have persisted for over two years following treatment. In other instances, more numerous, the rectal findings have shown definite improvement, but with persistence of some fixation and hardness. Subjectively, patients have shown improvement by cessation of sloughing and bleeding and greater ease of voiding associated with reduction of size of the local tumor mass.

A good number of the patients in this series already had extensive metastatic prostatic carcinoma and could not be expected to obtain more than temporary local benefit from the injection. These cases frequently had a bilateral orchiectomy performed at the same time as the gold injection, and are of little value in the final evaluation of the method. These cases of extensive disease have often obtained sufficient local improvement to make us feel that such treatment was worthwhile from a palliative standpoint. In addition, they are often very instructive as to the potential effects of the method. Autopsies of the 7 cases in this group have proved to be enlightening. Sections of prostate, surrounding infiltrating cancer and regional lymphatics show that distribution is no better than that obtained experimentally in the normal dog prostate. Wherever sufficient irradiation has been delivered, local destruction and healing by fibrosis has occurred; but this effect has not included the entire tumor mass, and there has been very little lymph node destruction. Lymph node pickup of radioactive material seems to be less than occurs experimentally, probably due to blockage of lymphatics by carcinoma.

We do not believe that we are able to evenly distribute lethal doses of irradiation by present methods of injection. This has been brought out not only by

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[5] Orr, L. M., Campbell, J. L. and Thomley, M. W.: Treatment of inoperable prostatic carcinoma by Au^{198}. J. Urol., 73: 1089–1095, 1955.

autopsy material, but also by post-injection biopsies which have all been positive with two exceptions. We believe that interstitial irradiation with radioactive gold is potentially an effective and safe method of destroying prostatic carcinoma, but, as employed at present, is not a curative method.

Radioactive yttrium has been used in only 5 patients, and our experience with this material so far indicates that results comparable to those obtained with gold are possible. Yttrium emits only beta irradiation of considerable energy and is much safer for patient and operator because of the absence of gamma rays. Although it is difficult to produce and obtain at present, we feel that further study is warranted. Experimentally, yttrium was found to distribute itself more completely in regional lymphatic tissue,[3] but we have had no opportunity to study this clinically so far.

Radioactive phosphorus, as employed in our 5 patients, has failed to give satisfactory results. Again, our experience is too brief to draw conclusions, but is definitely discouraging. The occurrence of a serious complication, possibly from bone marrow irradiation, has caused us to temporarily abandon its use.

The urinary levels of radioactive material indicate that in some cases as much as one-third of the injected dose is lost in the urine during the first 48 hours. Most of this loss is undoubtedly due to injection close to the urethra or into the urethra, and to excretion of radioactive material by way of prostatic ducts. The variability of urinary loss makes calculation of total dosage actually delivered to the prostate impossible. Urinary loss has been greater following the injection of small prostatic carcinomas because of the difficulty of holding even a small amount of fluid within a restricted area. Since dilution has been less in these cases, a small loss may include a good percentage of the total dose.

The maximal circulating blood levels following injection of all three isotopes indicate that a rather alarming amount of material may immediately be present within the bloodstream during the first few minutes following injection. This was particularly true in the case of chromic phosphate and yttrium chloride. The figures indicate the maximal circulating isotope, but are probably not indicative of true loss in the bloodstream due to incomplete dilution throughout the entire vascular compartment during the first few minutes. Actually, the total loss into the bloodstream is probably less than these figures indicate. Direct vascular injection may occur, although we are careful to aspirate the needles before injection. One patient who has thrombocytopenia and suppression of bone marrow function had 28.7 per cent of the total dosage of 33 mc. of radioactive chromic phosphate circulating in his bloodstream during the first five minutes following injection. Figures of blood level are not available on the second case with this complication. Although we cannot say at present that the present status of these 2 patients is due to irradiation damage, we are alarmed at the possibility that this may occur.

SUMMARY

About one-half of the patients with carcinoma of the prostate treated by injection of radioactive colloidal gold received some benefit.

Two patients out of a total of five injected with radioactive yttrium chloride received some benefit.

Five cases treated with radioactive chromic phosphate failed to show any improvement, and two of these patients have shown serious hematologic complications.

Urinary excretion of the injected isotope varied considerably and occurred chiefly during the first 48 hours.

Blood levels of isotope reached a peak within the first three minutes following injection, and were surprisingly high in some cases.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
Printed in U.S.A.

SERIOUS COMPLICATIONS ASSOCIATED WITH THE NEWER DIAGNOSTIC METHODS IN UROLOGY

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Urologists take pride in the undeniable fact that from a diagnostic standpoint their fascinating specialty is one of the most scientifically accurate.

With this firm conviction, new methods of diagnosis are adopted almost too ardently at times. This happens particularly if the new procedure has prospects of revealing a lesion not demonstrable with more conventional techniques.

Among the many new, well-established procedures introduced during the past decade, aortography and retroperitoneal pneumography are two of the most popular. These procedures have been used extensively enough and discussed in the literature sufficiently so that we can now adequately appraise their demonstrated value and manifest hazards. Unquestionably there are some potentially dangerous associated complications and this paper is primarily concerned with these unfortunate, alarming situations.

Retrorectal pneumography by the Ruiz-Rivas technique introduces a gaseous medium through a needle in the coccygeal region and it is designed to outline retroperitoneal organs and masses. Ordinarily the renal and adrenal contour can be appreciably shown by this method. This type of study has been particularly recommended for demonstrating tumors of the adrenal.

Perirenal insufflation is not new. It was first described by Carelli in 1921. Carelli introduced the medium through a needle puncture in the area of Petit's triangle and he was able to demonstrate the configuration of the kidney and surrounding retroperitoneal structures. For a short time the method became highly popular. However, several deaths from air embolism resulted and several instances of severe hemorrhage were also encountered and the intense enthusiasm was necessarily reduced. In spite of this several urologists are still persistent advocates. Cahill has employed the Carelli insufflation in over 500 patients without fatality.

Some surgeons unconditionally reject and unqualifiedly condemn this procedure. Where a tumor of the adrenal is suspected and not demonstrable by the more conventional techniques, this particular group would prefer to explore surgically rather than subject the patient to the danger of diagnosis by injection of the gaseous medium. Apparently from past experiences they have been thoroughly sensitized against the pneumographic method.

In order to overcome the serious complications of the Carelli procedure Ruiz-Rivas developed retrorectal pneumography. Using this technique, the operator introduces a spinal needle in the area of the coccyx. Under local anesthesia with a finger in the rectum, the needle is guided into the retrorectal space. A gaseous medium is then injected under pressure with a hand syringe. The mediums used

Read at annual meeting, Northeastern Section of American Urological Association, Lake Placid, N. Y. September 22–24, 1955.

have been air, oxygen, or helium. From 800 to 1500 cc are injected. After introduction of the medium the operator makes a roentgenogram with the patient in the reclining position. Ordinarily the gas rises in the retroperitoneal area and outlines the structures. The patient experiences only a slight discomfort and within a period of a few hours, the gas is absorbed. The rather mild discomfort has never been distressing enough to deter use of the procedure.

The resulting roentgenograms are interesting and possess a great measure of eye appeal. The adrenals, the kidneys, as well as any renal tumors stand out in almost three dimensional relief. However, any renal tumor which can be demonstrated by retroperitoneal pneumography is usually recognized by physical examination or by our more conventional diagnostic methods. Pneumography simply verifies our findings without adding knowledge as to the nature of the lesion. In the opinion of the writer, with the possible exception of demonstrating adrenal tumors, the method falls short of augmenting the diagnosis.

When first reported by Ruiz-Rivas in 1950, retroperitoneal pneumography enjoyed an immediate and extensive acceptance. Reassurances about its safety became clichés: "The retrorectal area is almost avascular so that danger from air embolism is negligible"; "embolism from oxygen is unknown"; "the method possesses advantages of simplicity, ease and safety." With such presumptuous attestation, urologists employed the procedure with almost reckless abandon. Some adapted it routinely with all pyelograms and aortograms. The resulting picture was indeed more impressive although not more enlightening than ordinary studies.

Like the original method of Carelli, the Ruiz-Rivas technique lost many of its advocates when reports of deaths began to appear in the literature. Deaths and near deaths were experienced with the use of oxygen, air and helium.

Dr. Reed Nesbit reported the first fatality in the August 1953 Urologist's Correspondence Letters. In the discussion, he first recalled a death in a 9-year-old girl during injection of air with the needle inserted below the twelfth rib according to the Carelli technique. Following this horrible experience, Nesbit discontinued the use of this diagnostic method for a period of 7 years. When the new procedure was introduced, he began employing it and met with another fatality. This occurred in a 54-year-old woman who was being studied for a possible pheochromocytoma suspected because of a very labile blood pressure. Eight hundred cubic centimeters of air were injected through a 20 gauge needle, "very slowly and with great ease," with the patient in the knee-chest position. The patient was removed from the table to a chair and in about five minutes, chest pain and deep cyanosis developed and she fainted away. She was given artifical respiration and cardiac stimulants but resuscitation failed. Autopsy showed a considerable amount of air in the heart chambers, in the coronary vessels and in the vessels of the brain. There was no evidence of any torn vessel in the pelvis or elsewhere which would identify the point of entry of the air into the vascular system.

In the same report, Nesbit related a case from the experience of his associate, Dr. Lapides. After injecting air into the retrorectal space, the man experienced syncope, thready pulse and the typical "mill-wheel" murmur over the precordium. He was given artificial respiration and survived although he was ill for the following 2 weeks. Such complications must be classed as near deaths because a substantial number of patients who reach this stage of air embolism die.

Breakey also reported a death of a child from air embolism following this type of study.

Bandell of Binghamton told of a death of a woman who was given helium as the gaseous medium under the same circumstances.

An instance of near death following oxygen insufflation through the presacral channel was reported by Russ, Glenn and Gianturco. This occurred in a 74-year-old woman after 500 cc of oxygen was introduced. The typical "mill-wheel" murmur developed but the patient survived after stimulants had been administered.

Undoubtedly many such complications have not reached the literature. Although the author has used this type of study many times without serious complications, he is not at all enthusiastic about it any longer.

Certainly such experiences should discourage anyone from using this type of examination for academic purposes or to develop a series. It is very difficult to justify death due to a diagnostic procedure. With the possible exception of an adrenal tumor, presacral pneumography cannot divulge a retroperitoneal tumor that cannot be demonstrated by our more conventional and much more safe techniques. Simply to reveal more effectively the outlines of a tumor on the roentgenogram, without adding additional information about its nature, is no justification for a method that carries with it such potentially serious complications.

Aortography is the second distinctly popular diagnostic method which has been adopted by urologists within the past decade. By this method a contrast medium is introduced into the aorta and renal lesions are diagnosed by noting the abnormal deviations of the renal vascular tree.

This was first described by Dos Santos in 1929. The pioneering work was done in this country by Doctors Nelson and Doss, working independently.

This type of study is very useful as a diagnostic procedure. When properly done, aortography can reveal renal lesions that are not demonstrable by any other of our conventional studies. Its greatest use is to differentiate between a cyst or a solid tumor of the kidney. In case of a cyst, the mass is avascular; in that of a solid tumor, the typical sinuses can be demonstrated on the x-ray film. Early renal malignancies can at times be detected. In the opinion of the author, aortography has a far greater value for diagnosis than pneumography.

When aortography was first reported, urologists were hesitant about accepting it. There was a dread of introducing a needle into the aorta.

According to the established technique, a 12 cm. needle gauged from 18 to 12, depending on the operator's choice, is used. With the patient in the prone position, usually under general anesthesia, the skin is pierced below the twelfth rib four finger-breadths to the left of the spinous process. The needle is advanced forward, medially and cephalad until it enters the aorta. Experience tells the operator when it has entered the lumen by the typical lack of resistance encountered at the time. When the stylet is withdrawn, a very active spurt of blood is noted. At this point, a syringe with the contrast medium is attached and twelve to twenty cubic centimeters of the dye are introduced under heavy pressure. The medium must be injected in two to four seconds in order to get a satisfactory picture, and the roentgenogram must be taken in 1/10 to 1/30 of a second. Unless done with this rapidity, the dye is dispersed and no worthwhile picture is obtained. The technique is not difficult and the resulting study is a very interesting and impressive one.

The needle usually enters the aorta above the coeliac axis and the aorta with its branches are effectively outlined. Below the coeliac axis are the renal arteries and it is from their study that lesions in the renal parenchyma can be diagnosed.

When aortography was first introduced, 80 per cent sodium iodide was the medium most frequently used. Several deaths resulted when the dye was accidentally introduced into the superior mesenteric artery instead of the aorta. Because of the severe irritating effects of the high concentration of sodium iodide, mesenteric thrombosis occurred with the resulting inevitable fatality. This danger was first overcome by an initial injection of only 2 cc of the dye, noting in the resulting picture the position of the needle and then proceeding. Later, through the work of Parke Smith, it was shown that satisfactory aortograms could be made with organic iodides. Even if the dye were accidentally injected into the superior mesenteric artery, no serious complications from this previously hazardous technique have probably been eliminated.

Miller, Wylie and Hinman reported damage to the kidney in 7 instances following translumbar aortography. In some of these cases the damage to the kidney was made by a misdirected needle entering the renal artery with the mass of dye injected into the left renal artery. In one of their cases, permanent damage was manifested by renal atrophy.

One of the most serious and terrifying complications of translumbar aortography is the occurrence of paraplegia. This was first called to our attention by Nelson in a discussion of a paper at the 1950 meeting of the American Urological Association. He related a case which had been reported to him while on his trip to Europe. At the time that this was mentioned, most of us dismissed the incident as something very unusual and probably the result of an inexcusably clumsy operator. However, Nelson told me of another case which came to his attention that occurred somewhere in Canada. He had very little data on any of these patients. In 1953, Abeshouse had a similar complication following translumbar study in a patient with hypernephroma. Later in 1954, Boyarsky reported a case of paraplegia following translumbar aortography. He stated that "only after six or eight attempts was the aorta punctured." He also stated that no spinal fluid or gas escaped through the needle. When the patient recovered fully from the general anesthetic, he was unable to move his legs and examination showed flaccid paralysis of the lower extremities. Study of the spinal fluid showed no increase in pressure and no abnormal cellular elements. About three months after aortography, the patient was able to walk with the aid of crutches.

In Boyarsky's article, he mentioned another case of paraplegia following translumbar aortography reported by Antoni and Lindgren.

We sometimes sit back complacently and believe that this terrifying, unexplainable, rare complication can happen only to the other fellow. However, in spite of such an attitude, I recently came in much closer contact with this perplexing condition. While I was on vacation, a 68-year-old woman was studied by the urologic service because of a mass in the right flank. Examination showed a tumor possibly associated with the right kidney. Aortography was indicated, and an associate, who is thoroughly experienced in the translumbar technique, made the study in my absence. The operator had some difficulty and made several punctures before the needle was introduced into the aorta. The aortogram showed definitely that the mass was a cyst. After recovering from the anesthetic the patient was unable to move her legs. On my return, I examined the patient and noted that motor and pain perception in her lower extremities were gone. She retained touch sensation. Our neurologist stated that the lesion was due to thrombosis of the anterior spinal artery. The paraplegia had been present without change for 3 weeks. Otherwise, the patient seemed perfectly well. On the day she decided to go home, she felt ill, had a temperature of 103F, and very rapidly and unexpectedly died. A definite cause of death was not apparent. No postmortem examination was permitted.

This makes a total of 6 instances of this horrible complication which has come to the attention of the author and there are, undoubtedly, others unreported. That there are six such cases makes the complication not an incidental one.

The method by which air embolism occurred in the retrorectal injections and the exact cause of the thrombosis that produces paraplegia in translumbar aortography are not known. Because of this, we can only conjecture and for the same reason it is difficult to devise methods of prevention.

After the tragic reports in connection with the retroperitoneal studies, we have abandoned such studies except in rare instances. The only indication that we recognize is to demonstrate a possible tumor of the adrenal. Any other lesion that is demonstrable by this method is more easily and more safely diagnosed by the more conventional methods.

Although Parke Smith has done over one thousand translumbar aortographies without serious complications, we believe that the operator should exercise utmost caution in the selection of his cases and the performance of the technique. This valuable diagnostic procedure should not be abandoned. With this type of study we can demonstrate lesions that cannot be found by our usual type of examination. However, in no instance should aortography be performed when the nature of the lesion can be revealed by more orthodox examinations.

After an experience of 4 years with a fairly large series of translumbar aortographies, we began to use the method of catheterizing the femoral artery. For the past 2 years, aortographies have been done at the Guthrie Clinic in this manner in order to avoid the complications of the translumbar method. The method is comparatively simple, requires no general anesthesia and resultant studies are at least as good as those done by the translumbar method.

We entertained the idea that the serious complications were caused by mechanical trauma of the needle. Aortograms by the femoral route appeared to offer a method free from this type of danger. However, the writer was much confused when Dr. Wm. Parry of the Veterans Administration Hospital in Syracuse reported the case of a patient who suffered paraplegia following aortography after a femoral study.

In conclusion, it is the author's impression that the Ruiz-Rivas method of air study can almost be discarded in the average clinic. Indications for its use are rare. Aortography has a definite place in the urologic armamentarium. However, it should be used only where a lesion is suspected and cannot be demonstrated by one of the more conservative methods of study.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
Printed in U.S.A.

THE TREATMENT OF MALE INFERTILITY WITH ESTROGENIC SUBSTANCE

WALTER M. KEARNS

For many years a multiplicity of agents were employed in futile efforts to stimulate spermatogenesis, which proved to be a most unimpressionable physiological process. The approach to this problem has been modified by recent developments. First a temporary depression of spermatogenesis is produced. Recovery invariably follows and with it a quite consistent improvement in the sperm output.

Early experience with the clinical use of testosterone[1] showed us that during the administration of this potent substance to normal young men a depression of androgenic activity was apt to develop as long as treatment was continued. Recovery followed withdrawal. Heller and Nelson[2] and their associates demonstrated a depression of testicular activity and degenerative histological changes with the administration of testosterone. These changes proved to be reversible as recovery followed withdrawal. Heckel and McDonald[3] administered testosterone for varying periods which were followed by improved fertility in a number of patients. Their groundwork is the basis for the use in many centers of the so-called rebound treatment. Accumulating evidence attests to the safety of this method in properly selected patients.

The idea to pursue another tactic resulted from the observation that several patients who received estrogens for the treatment of prostatic carcinoma and who later neglected treatment experienced a resumption, to a degree, of sexual activity.

The advisability of administering an estrogen instead of an androgen to infertile young men was considered. Estrogens are not foreign substances but are normally present in the male in measurable amounts in the testes and urine. In fact the richest natural source appears in the urine of the stallion. When an estrogen is given in sufficient amount it acts, possibly through pituitary depression, as an antagonist of an androgen; in smaller amount it may act as a pacemaker of androgenic activity.

A search of the literature unearthed only one reference to the use of estrogens, that of Dunn and Charney,[4] who reported their experience with two rapist pris-

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Read at annual meeting of North Central Section of American Urological Association, Chicago, Ill., September 29–October 1, 1955.

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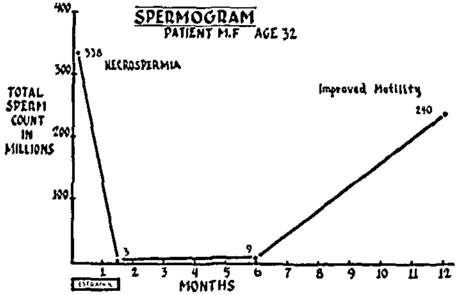

Fig. 1

oners to whom they gave 5 mg. of stilbestrol daily for 60 and 90 days respectively. *Their treatment was given solely for the purpose of relieving sexual mania.* Impotence and aspermia promptly developed. Testicular biopsies showed tubular degeneration, hyalinization of the basal membrane and absence of Leydig cells. When the estrogen was withheld histological and functional recovery was demonstrated in 9 and 16 weeks, respectively. These changes are practically identical to those described following treatment with testosterone.

Our first patient with infertility was treated by estrogenic substance in October 1950. A 32-year-old husband in a childless marriage of 7 years duration was given 0.5 mg. of ethinyl estradiol* twice daily for a period of 30 days for necrospermia. There resulted a depression of the total sperm count from the pretreatment level of 338 million to 30 million 2 weeks following treatment and a further depression to 6 million 6 weeks after treatment. At the expiration of 6 months the count had improved very slightly to 9 million. This led me to become wary and to discontinue further use of the estrogen although recovery followed.

One year later it was learned that this patient became the father of a baby boy about 18 months after the administration of the estrogen. Review of his record showed that the last count obtainable, at about the time of the onset of pregnancy, was 240 million with motility in 50 per cent of the forms (fig. 1).

Since then 37 patients have been treated. Practically all were referred by gynecologists who had studied their mates. All were private patients who were fully informed that they were participating in a new form of treatment. Control over these patients in office practice is limited as compared to the control of patients treated in prisons and mental institutions. Consequently the investigation was limited to the routine examination of the ejaculate including sperm cell counts and notation of motility and morphology. It was believed that their continued co-operation might be hindered if they were subjected to periodic removal of sufficiently sizable specimens of testis for histological study with the risk of further damaging already inefficient testes. Bayle[5] has reported obstruction of the vasa efferentia in 7 patients. He believes the cause to be the small but inevitable hemorrhage caused by biopsy. Others note that adhesions between the incisional area and the parietal tunica vaginalis occur as well as more diffuse inflammatory reactions. Intermittent bilateral biopsies cannot be done with impunity or without expectancy of some damage to the testes. The difficulty of interpretation and correlation of histological structures did not add an incentive for biopsy studies without the aid of a well organized fertility study center.

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* Estinyl was supplied by Dr. George Babcock Jr. of the research department of Schering Corporation.

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Likewise the young low-income worker, treated as an outpatient, must often forego repeated urinary gonadotrophin tests because of the expense and the lack of a ready supply of young animals at the laboratories of local private hospitals. The test itself, showing a considerable variable, is not an infallible indicator of pituitary activity and may justifiably be omitted as a prerequisite to the institution of an innocuous treatment. Its harmlessness, as judged by all available clinical evidence, is probably due to the short deviation and moderate dosage employed.

The essential histology lies in the end product—the ejaculate—the examination of which is simple and causes little inconvenience. The prompt recovery of potency and later improved sperm count give better assurance of recovery than biopsy evidence. By proceeding cautiously in this manner it was believed that this first step in the study would serve as a justifiable basis for more thorough tests in a later series.

Six patients with azoospermia were treated without benefit; they are candidates for biopsy and study of ductal patency.

It was possible to follow 24 of the others who had either necrospermia or oligozoospermia or both. Each patient received an identical dosage of 0.5 mg. ethinyl estradiol twice daily for one month. All other medication was omitted. This set regimen was adhered to in an effort to establish the effect of a certain given dosage with respect to safety and possible late ill effects.

Upon withdrawal of the estrogen there apparently occurs functional overreaction following the inhibition of testicular hormone production. Spermatogenesis returns and in the majority of patients an improved sperm output results. There were 8 pregnancies and two miscarriages in a ninth patient (see table 1 and fig. 2).

Five patients failed to completely regain their former total sperm count (table 2).

The motility in the pre-treatment ejaculate was compared with that in the latest post-treatment test. In 18 there was improvement, in 4 there was dimin-

TABLE 1. *Summary of 24 patients with tests covering a minimum of 4 months*

Number of pregnancies (childless 2 to 7 yrs.)	8
Improvement in sperm count	19
Failure to attain original count (4–13 mos.)	5
Av. time to attain max. count	10.3 mos.
Av. time for return of potency	2.5 wks.
Reduction of sperm count to zero (6 pregnancies)	9

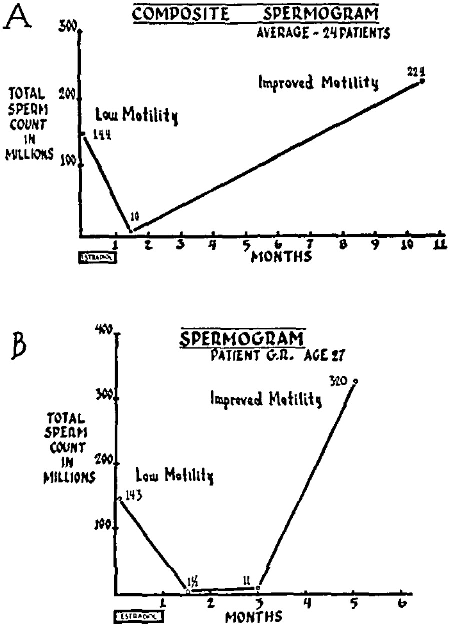

FIG. 2. *A*, composite spermogram. *B*, spermogram of G. R., aged 27, depicts most rapid recovery in series.

TABLE 2. *Failure to regain pre-treatment total sperm count*

Patient	Age	Pre	Post	Time in Mos.
M. F.	32	338	240	13
B. P.	38	325	280	5
A. F.	23	41	28	12
B. F.	30	178	146	4
J. W.	37	45	42	5

Average age, 32.0 yrs.; average age of 19 others, 27.7 yrs.

ished motility and in 2 it was unchanged. These ratings are subject to criticism because insufficient time elapsed for recovery in some patients. Moreover, the indifference of some patients, religious restrictions and distance from the office, causing tardy delivery of specimens, all mitigate against more ideal test conditions.

There was no noteworthy change in the percentage of immature and abnormal forms in a comparison of the pretreatment and post-treatment specimens.

The volumes of the semen immediately following treatment were consistently tion of the vasa efferentia in 7 patients. He believes the cause to be the small but inevitable hemorrhage caused by biopsy. Others note that adhesions between the incisional area and the parietal tunica vaginalis occur as well as more diffuse inflammatory reactions. Intermittent bilateral biopsies cannot be done with impunity or without expectancy of some damage to the testes. The difficulty of interpretation and correlation of histological structures did not add an incentive for biopsy studies without the aid of a well organized fertility study center.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
Printed in U.S.A.

A COMPARATIVE STUDY OF PHOSPHATASE ACTIVITIES OF VARIOUS HUMAN TISSUES

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The desirability of concentrating estrogenic substances in prostatic tissue as a means of cytostatic repression of prostatic carcinoma led Druckrey and Raabe[1] and Huggins[2] to suggest the parenteral use of diethylstilbestrol diphosphate in the hope that estrogen would be deposited in situ by the action of prostatic phosphatase. Clinical results from the use of this compound in prostatic carcinoma have been encouraging in a number of cases.[3] The favorable action of diethylstilbestrol diphosphate, however, might be accounted for by its general estrogenic effect and ease of tolerance in large doses rather than by any specific action of prostatic phosphatase, by which it is in fact poorly hydrolyzed. Bioassay of estrogenic activity in the human tissues after administration of diethylstilbestrol diphosphate revealed that such localization as had occurred in the prostate was small and transient.[4]

The basic question as to whether or not the acid phosphatase of human prostatic tissue is sufficiently active at physiological hydrogen ion concentrations to hydrolyze circulating orthophosphoric acid esters of cytostatic or cytotoxic substances remains to be answered. Although a high concentration of acid phosphatase is characteristic of adult human prostate, it is necessary to evaluate the competitive action of phosphatases in nonprostatic tissues. An earlier comparison by Woodard[5] of the pH optima of human osseous and prostatic phosphatases with β-glycerophosphate as substrate indicated that, on a weight basis, prostatic tissue was the more active at pH 7. Reis[6] similarly found that the hydrolytic activity of prostate was many times greater than other human tissues at pH 7.5 toward phenyl phosphate.

The present study was carried out to reinvestigate the phosphatase activities at different pH's of various human tissues including benign and malignant (primary and metastatic) prostatic tissue with particular reference to physiological pH ranges.

Accepted for publication January 26, 1956.

This investigation supported by U. S. Public Health Service Grant N. C-2044, administered by R. H. Flocks, M.D.

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MATERIALS AND METHODS

The normal and pathological tissues which were studied are listed in the tables. The determination of tissue phosphatase of bone, nervous and sensory tissue was not attempted. Normal prostatic tissue was not available.

Enzyme assays of the nontumorous tissues were made individually or on pooled samples from various patients.* The material obtained from the operations was immediately frozen and kept at −10 degrees C until assayed. The tissues were sliced in the cold with a Stadie-Riggs microtome and were extracted by the procedure of London and Hudson.[7] The phosphatase content of the extracts toward sodium phenyl phosphate was carried out using the King and Armstrong method[8] as modified by Fishman and Lerner,[9] incubating in 0.01 M sodium acetate and veronal buffers[10] covering a pH range from 2.5 to 9.1. The nitrogen content of the extracts was determined by direct nesslerization according to the method of Vanselow[11] after wet digestion.[12] The results are reported as milligrams of phenol liberated per milligrams of nitrogen per hour at 37°C with 0.01 M disodium phenyl phosphate.

In certain instances the tissue extracts were also assayed for phosphatase content by incubating with 0.01 M sodium β-glycerophosphate according to the Bodansky[13] modification of the method of Fiske and Subbarow[14] using the same series of buffers as used with the King-Armstrong method.

RESULTS

The phosphatase activity of the prostate and related specimens is shown in table 1. A comparison of the data with those shown in succeeding tables points out the magnitude of the concentration of phosphatase in human prostatic tissue, particularly in benign hypertrophy. The estimated mean activity of the extracts of the four samples of benign tissue from elderly patients was 210 mg. phenol/mg. N/hour at pH 5.0. This activity was of the same order of magnitude as that of a partially purified extract of an entire prostate removed from an elderly patient.

The enzyme activities of malignant prostatic tissues were, in most cases, less than those of the benign. The phosphatase of metastatic tissue from prostatic

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* We are indebted to the Departments of Obstetrics and Gynecology, and Surgery for providing some of these specimens.

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TABLE 1 *Phosphatase activities of prostatic extracts and secretions at various hydrogen ion concentrations*

Specimen	Patient	pH													
		2.6	3.7	4.3	4.8	5.0	5.2	5.5	5.7	6.1	6.9	7.4	7.9	8.5	8.9
Prostate, benign	A	0	130	154	165	174	1	182	—	168	120	33	5	0	0
Prostate, benign	B	9	224	283	296	—	380	—	323	—	151	16	7	0	0
Prostate, benign	C	0	51	60	62	61	—	62	—	78	50	6	0	0	0
Prostate, benign	D	7	229	273	259	296	—	—	294	—	147	22	4	0	0
Prostatic extract	M	—	112	150	—	171	—	169		136	98	39	9	0	
Prostate cancerous	F	—	—	4.6	5.2	—	5.5	—	4.8	—	2.4	0.6	0.1	0	0
Prostate cancerous	I	0	17	19	22	22	—	23	—	22	12	4	1	0	0
Prostate, cancerous	G	0	18	21	23	22		23		26	15	3	0	0	0
Prostate, cancerous	H*	2	62	73	80	—	84	—	82	—	37	4	1	0	0
Prostate, cancerous	H†	0	30	46	49	—	50	49	—	49	35	6	1	0	0
Primary prostatic tumor	J	0	65	73	79	87	—	88	—	78	53	13	12	0	0
Metastatic lymph node	I	0.9	3.4	3.6	3.3	3.6	—	3.5	—	3.5	3.4	2.2	0.3	0	0
Metastatic lymph node	II	0.1	0.7	0.8	0.9	0.9	—	0.9	—	0.9	0.6	0.1	0	0	0
Primary prostatic tumor	K	0	0.16	0.17	0.19	0.19	—	0.14	—	0.19	0.05	0	0.02	0	
Liver metastases	K	0	0.60	0.62	0.62	0.57	—	0.57	—	0.37	0.05	0.07	0.15	0.25	
Prostatic sarcoma	L	0	6.3	8.2	8.4	8.8	—	—	7.7	8.7	1.8	1.4	0	0	
Semen		0	328	656	656	702	686	—	—	679	318	88	5	0	
Semen		0	165	325	322	341	341	—	—	327	140	44	3	0	
Semen		0	164	236	212	252	225	—	—	232	106	27	3	0	
						←optimum pH range→									

* Capsule

† Dissected tumor

TABLE 2. *Phosphatase activities of extraprostatic genital and gastrointestinal tissue extracts at various hydrogen ion concentrations*

Tissue	pH													
	2.6	3.7	4.3	4.8	5.0	5.2	5.5	5.7	6.1	6.9	7.4	7.9	8.5	8.9
Seminal vesicles	0.01	0.67	0.75	0.73	—	0.69	—	0.56	—	0.21	0.05	0.02	0.01	0
Ampulla	0.08	0.41	0.44	0.44	—	0.40	—	0.29	—	0.12	0.05	0.01	0.01	0.01
Epididymis	0.04	0.19	0.17	0.13	—	0.20	—	0.12	—	0.01	0	0	0	0
Epididymis	0.14	0.56	0.56	0.56	0.56	—	0.28	—	0.85	0.14	0	0	0	0.14
Penis, corpus	0.05	0.46	0.42	0.41	0.39	—	0.46	—	0.47	0.09	0.08	0.02	0	—
Penis, corpus, carcinoma	0.13	0.25	0.26	0.25	0.23	—	0.16	—	—	0.08	—	—	—	—
Foreskin	0.06	0.68	0.82	0.82	—	0.99	—	0.79	—	0.34	0.06	0.04	0.08	0.09
Testis	0.00	7.04	8.76	8.76	—	9.25	—	8.65	—	4.13	0.49	0.25	0.06	0.06
Testis	0.07	11.0	11.2	11.5	11.5	—	—	10.8	—	5.1	0.09	0.3	0.1	0
Testis	0.00	0.66	0.71	0.68	0.79	—	0.66	—	0.42	0.00	0.09	0	0	0
Uterus	0.05	0.19	0.18	0.17	0.18	—	—	0.13	—	0.05	0.07	0.06	0.07	0.08
Uterus	0.06	0.10	0.06	0.08	—	0.07	0.06	—	0.04	0.00	0	0	0	0
Uterus	0	0.05	0.05	0.05	0.05	—	—	0.04	—	0	0	0	0	0
Uterus, fibroma	0.04	0.15	0.14	0.14	0.12	—	—	0.10	—	0.04	0.02	0.02	0.02	0.04
Tubes	0.00	0.28	0.33	0.33	—	0.31	0.28	—	0.21	0.11	0.03	0	0	0
Cervix	0.01	0.11	0.12	0.11	—	0.12	—	0.08	—	0.03	0.02	0.04	0.01	0.01
Cervix	0.00	0.13	0.15	—	—	0.16	0.13	—	0.12	0.06	0	0	0	0
Vaginal wall	0.01	0.14	0.16	0.19	—	0.21	0.20	—	0.20	0.12	0.04	0	0	0
Ovaries	0	0.18	0.20	0.19	—	0.19	0.16	—	0.13	0.04	0.02	0	0	0
Gastric mucosa	0.04	0.25	—	0.22	—	0.24	—	0.17	0.11	0.03	0.03	0.01	0	0
Gastric ulcer	0.03	0.04	0.34	0.30	—	0.28	—	0.22	0.24	0.02	0.06	0	0	0
Gastric carcinoma	0.00	0.33		0.31		0.26	0.22	—	0.16	0.05	0	0	0	0
Jejunum	0.03	0.21	0.24	0.24	0.24	—	0.21	—	0.37	0.18	0.21	0.49	—	1.21
Colon	0.02	0.37	0.37	0.33	0.33	—	0.26	—	0.19	—	0.02	0.02	0	0
Colon, carcinomatous	0	0.15	0.16	0.16	0.19	—	—	0.12	—	0.03	—	—	—	—
Gallbladder .	0	0.19	0.22	0.22	—	0.19	0.16	—	0.10	0.04	0	0	0	0

TABLE 3 *Phosphatase activities of extragenital tissue extracts at various hydrogen ion concentrations*

Tissue	pH													
	2.6	3.7	4.3	4.8	5.0	5.2	5.5	5.7	6.1	6.9	7.4	7.9	8.5	8.9
Lung	0.05	0.69	1.09	—	1.36	1.40	—	1.43	1.09	0.47	0.19	0.06	0.11	0.19
Lung	0.23	0.50	0.61	0.74	0.81	—	—	0.75	—	0.31	0.19	0.16	0.17	0.20
Breast mastitis	0	0.03	0.03	—	0.03	0.03	0.03		0.07	0.01	0.01	0.01	0	0.03
Breast, cancer	0.11	0.94	0.93	0.92	0.87	—	—	0.61	—	0.38	0.03	0	0	0
Breast cancer	0.05	0.18	0.21		0.21	0.16	0.11	—	0.09	0	0	0	0.09	0.23
Pancreas	0	0.78	0.83	0.76	—	0.73	0.61	—	0.34	0.15	0.06	0	0	0
Liver	0	0.55	0.80	0.74	—	0.73	0.58	—	0.30	0.14	0.08	0.05	0.08	0.16
Spleen	0.02	0.50	0.55	—	0.50	0.45	—	0.40	0.27	0.04	0.05	0	0	0
Spleen (obstructed)	0.04	0.19	0.35	—	0.15	0.15	0.08	—	0.19	0	0	0	0.04	—
Kidney	0.03	0.57	0.57	0.58	0.58	—	0.52	—	0.39	0.13	0.10	0.03	0.13	0.27
Bladder diverticulum	0.17	0.16	0.18	0.18	0.20	—	—	0.17	—	0	0.03	0.03	0.08	—
Heart	0.00	0.09	0.09	—	0.09	0.09	0.06	—	0.08	—	0	0	0	0
Veins	0.03	0.06	0.07	0.13	0.11	—	—	0.11	—	0.04	0.02	0.01	0.02	0.02
Muscle	0.01	0.04	0.05	—	0.06	0.06	—	0.04	0.03	—	0	0	0	0.01
Fat	0	0	0.13	—	0.11	0.08	0.05	—	0.08	0.00	0.01	0.02	0.05	0
Skin	0	0.52	0.54	0.54	0.51	—		0.47	0.32	0.14	0.02	0	0	0
Skin	0	0.15	0.18	—	0.18	0.18	0.15	—	0.14	0.03	0.03	0	0	0.03
Hernial sac	0	0.03	0.04	0.04	0.04	—	—	0.04	0.07	0.02	0	0	0.02	—
Pleura	0.03	0.11	0.11	0.11	0.11	—	—	0.10	0.07	0	0.01	0.01	0.02	—
Adrenal	0	0.66	0.66	0.75	—	0.69	—	0.49	0.27	0.13	0.08	0.08	0.17	0.35
Thyroid adenoma	0	0.44	0.48	—	0.50	0.41	—	0.40	0.11	0.09	0.09	0.03	0.02	0.02
Thyroid adenoma	0	0.10	0.11	0.10	—	—	—	0.10	0.07	0.03	0.01	0	0	0

TABLE 4. *Comparison of action of various tissue extracts toward phenylphosphate and glycerophosphate*

Tissue*	Optimum pH		Hydrolysis Rate† $\frac{\text{Phenyl-PO}_4}{\text{Glycero-PO}_4}$
	Phenyl-PO_4	Glycero-PO_4	
Prostate, benign (2)	5.2	5.2	1.70
Prostate, malignant (3)	5.4	5.1	1.90
Testis (2)	5.1	5.2	1.97
Penis, cancer	4.3	4.7	1.85
Seminal vesicle	4.3	4.5	2.28
Cervix	5.2	5.4	2 66
Tubes	4.5	5.0	2.72
Breast, cancer	3.8	4.7	1.36
Gastric mucosa	3.7	4.4	2.05
Gallbladder	4.5	4.9	1.57
Skin	4.5	4.4	1.98

* Figures in parentheses refer to number of specimens averaged.

† Calculated from moles of substrate split per mg. N per hour.

carcinoma was still less than that of the primary tumor. Tissue from patient K obtained at autopsy was highly dedifferentiated and had a low phosphatase content. Metastases were found only in liver. They also had low enzyme content. Prostatic sarcoma tissue had a low phosphatase activity as compared with most other prostatic specimens studied. The high activity found in semen may be explained on the basis of the sexual stimulation of phosphatase production which obviously attended the semen collection.[15] The pH optima of semen and all types of prostatic extracts were 5.0–5.5. Although only a few samples were available, metastatic tissues and highly dedifferentiated malignant tissues appeared to have a pH optima at a more acid range.

Table 2 lists the phosphatase activities of male (extraprostatic) and female genital tissues. It will be noted that testes in 2 cases out of three had a significant content of phosphatase with a pH optimum at about pH 5. Possibly these cases reflect different degrees of testicular function as a result of previous treatment. The activities of other tissues were low. Although measurements of low phosphatase activities were less precise, the extracts having low activity generally had pH optima much more acid than those observed with prostatic phosphatase. A similar conclusion can be drawn from the data in table 3. With the exception of the lung, the tissue extracts had low enzyme activity, even at pH ranges in which alkaline phosphatase activity is measured. Gastrointestinal, parenchymous, vascular, supportive and endocrine tissues in general exhibited phosphatase pH optima from 4.3–5.0. The acid phosphatase of lung tissue was, in the 2 cases studied, the most active of the nongenital tissues and had pH optima in roughly the same range as prostatic phosphatase.

In order to compare the activities of the various tissue phosphatases against phenyl phosphate and β-glycerophosphate, the position of the optimum pH peak and the relative phosphatase activity of the tissue extracts are listed in table 4.

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The position of the pH optimum observed with phenyl phosphate was essentially the same as with glycerophosphate in the case of prostatic, testicular, gastrointestinal and bladder extracts The deviations observed between pH optima for the substrates observed in the other tissues of low activity may well be due to experimental error

DISCUSSION

Acid phosphatase was found to be widely distributed among all of the tissues examined Of the various tissues studied, the prostate contained by far the greatest phosphatase activity in the range from pH 3 0-8 0 Our data confirm the observation by Woodard[16] that the phosphatase content of malignant prostatic tissue is lower than that of benign Unfortunately normal prostatic tissue was unavailable for comparison Production and excretion of the prostatic fluid which contains acid phosphatase appears to be a well regulated mechanism in the normal organ In the pathological state the control of the production and secretion of the enzyme into the canalicular space may be disturbed

The difference in phosphatase activities between malignant and benign hyperplastic prostatic tissue might be explainable on the basis of the large amount of enzyme stored in the ducts and collecting sinuses It may well be that the amount of intracellular phosphatase in benign tissue is less than appears at first glance, and is probably less than the amount in early malignant cells Gomori[17] and Downey[18] demonstrated histochemically that the carcinomatous cells were rich in enzyme whereas in benign hypertrophy the enzyme was found chiefly in the canalicular space and an adjacent layer of epithelial cells The wide variation in phosphatase content of soft tissue metastases of prostatic origin is not surprising in view of the variable degree of dedifferentiation of these tissues Explants of prostatic tissue did not cause a rise of serum acid phosphatase, even though histochemically the enzyme content was high[19]

The phosphatase content of the nonprostatic tissues studied was generally low Of these, lung and testis (two out of 3 cases) had an appreciable amount of acid phosphatase Unfortunately bone tissue, a rich source of alkaline phosphatase, was not readily studied by the present technique

There appear to be a multitude of phosphatases in animal tissues,[20] each capable of hydrolyzing orthophosphate monoesters The hydrolysis of phenyl phosphate by crude tissue extracts must represent the sum of the actions of the component phosphatases present Since few individual members of this class of enzymes have been purified,[21, 22] little comparative information is available concerning their substrate specificities, cofactors, stability toward inactivating agents and optimum pH ranges. Probably marked differences exist. Acid phosphatases from different sources do not hydrolyze different esters with the same relative facility[23, 24] and their pH optima may be significantly different.

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The present data strongly suggest that qualitative differences between phosphatases of various tissues exist, as judged by the optimum pH of activity of the individual tissues extracts. The acid phosphatases of prostate and lung had a pH optimum at about 5, possibly denoting a similar complex of enzymes in both tissues. In marked contrast, the acid phosphatases of the parenchymatous, gastrointestinal, endocrine and genital (extraprostatic) tissues had a more acid optimum pH, suggesting a qualitative difference of these phosphatases from the prostatic. Indeed, in markedly dedifferentiated carcinoma of the prostate and in metastatic nodes, the decrease in total phosphatase content appeared to be accompanied by a shift in the pH optimum to a more acid range, implying the replacement of one type of acid phosphatase by another. Schwartz, et al.[23] have reported presumptive evidence for this view in a comparison of the relative activity toward two different substrates by normal and carcinomatous tissue extracts.

Whatever the functional importance of acid phosphatases of either prostatic or nonprostatic tissue, they very probably function at a pH different from the pH at which they are most active.

A comparison of the phosphatase activities of the various tissue extracts at pH 7.0–7.6 is revealing. In agreement with the findings of Reis,[6] the phosphatase activity of prostatic tissue was many fold greater than that of any other tissue studied although possibly certain foci in osseous tissue and choroid plexus may have a similar activity in this pH range.

As a result of these studies, we conclude that the possibility of utilizing prostatic phosphatase to achieve chemotherapeutic concentration of substances administered in the form of phosphate esters deserves further attention. Other investigations bearing upon this question are to be reported elsewhere.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
Printed in U.S.A.

THE APPLICATION OF ULTRASONIC ENERGY TO URINARY AND BILIARY CALCULI

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Our belief that calculi in the human body might be disintegrated or otherwise beneficially affected by ultrasonic energy was prompted by a number of reports on the use of ultrasonic energy in industrial testing methods, and by reports of scattered experiments with ultrasonics in physical, chemical and biological reactions.[1-15] Since the formation, or at least the growth, of calculi in the body appears to be a process of crystallization upon a nucleus, which may itself be composed of crystalline material, it was our hope that the proper application of ultrasonic energy could produce vibrations within the calculus which would be great enough to overcome the adhesive power of the smaller units of structure, so that dissolution of the calculus would result. Until our investigation was begun in 1948, this problem had apparently received no attention.

HISTORICAL BACKGROUND

Langevin's efforts, in 1917, to use high frequency sound waves in the underwater detection of submarines may be said to have initiated the science of ultrasonics. In the course of his experiments, using quartz crystals activated by the Poulsen arc, Langevin noted such phenomena as the cavitation effects on ocean waves and the lethal effects of ultrasonic energy on small marine life

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Accepted for publication December 21, 1955.

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A high point in the development of ultrasonic science came in 1930 when Wood, Loomis, Harvey and Hubbard[8, 14, 15] presented the results of several years of investigation and summarized the facts then known about ultrasonics. Where other investigators, using Rochelle salt crystals or magneto-striction type generators, had found their output limited to about 50,000 cycles per second, Wood and his colleagues, with an apparatus consisting of quartz crystals activated by a vacuum tube oscillator, had been able to develop frequencies as high as 500,000 cycles per second. With their apparatus, they had been able to produce emulsions of ordinarily immiscible substances like mercury and water, and they had caused glass rods to burn holes in wood. They had found, too, that because air is a very poor conductor of ultrasonic energy, this energy is almost completely dissipated as heat at a liquid-air interface. As a result, they had been able to devise a means of measuring ultrasonic output by determining the heat produced at such a barrier. Of particular medical interest, however, was their report on the turbulent motion produced within a cell exposed to ultrasonic energy.[15] Such exposure, they reported, resulted in complete mixing of the cell content, but if the cell membrane remained intact, the protoplasm resumed its initial structure and differentiation when the ultrasonic treatment was terminated.[8]

Later studies culminated in such diverse applications of ultrasonic energy as the sonar of World War II;[16] the rapid testing for flaws in metal castings;[1, 6, 7, 17] the coagulation of mine dust to prevent explosions[5, 18] and the rapid cleansing of small machine parts.[19] In Germany particularly, ultrasonic diathermy has been applied for treatment of deep seated inflammations, with reported success,[11, 12, 20-22] but medical applications otherwise have been few.

TRANSMISSION OF ULTRASONIC ENERGY

In general, one thinks of sound as audible waves of vibratory energy in air, the source of which is the vibration of some mechanical body. It has been established that the normal human ear can detect frequencies up to about 18,000 cycles per second.[3, 9, 16, 19, 23] Above this frequency, the vibrations become inaudible and are termed ultrasonic. Frequencies as high as 500 million cycles per second have been developed experimentally.[16]

Ultrasonic waves need material media in which to travel and the transmission of ultrasonic energy depends largely on the elastic properties of the transmitting medium.[1, 4, 7, 19] It has been determined that water, oil and mercury make good coupling between the vibrating head and the object to which energy is to be

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transmitted[14] [15] As Wood and his colleagues had found, however, air pockets or bubbles block energy transmission almost completely, and the energy is dissipated as heat In general, ease of energy transfer between two media depends on the difference in specific acoustic impedance between two materials Acoustic impedance is defined as the product of the density of the material and velocity of sound through it The velocity of sound in water, for instance, is 1 49 × 10^5 cm per second Since the density of water is 1 gram per cubic centimeter, the product of sound velocity and density gives a specific acoustic impedance of 1 49 × 10^5 grams per square centimeter per second Muscle, fat and glandular tissue have acoustic impedance within 15 per cent of that of water (1 54 gm /sq cm /second was the mean value determined by Ludwig in his studies on gallstones)[10] For our experiments then, water seemed a satisfactory medium in which to test the possibility of ultrasonic disintegration of calculi before any clinical application was attempted

A piezo electric crystal is the usual source of ultrasonic energy in the laboratory[16] The mounting and facing of a properly cut and ground crystal are critical in obtaining an efficient transfer of energy Energy transfer from the vibrating crystal to the test specimen is analogous to a boxer striking a punching bag As the frequency of the blows increases, the bag strikes the board more rapidly, and the speed of the bag becomes greater until it seems to be motionless and the pressure against the board seems to be constant At high frequencies, the alternating particle stress is so rapid that there is not time for movement, or, as one authority has put it, "It is all acceleration and no motion "[19] At an intensity of 6 watts/sq cm alternating pressures of ±4 atmospheres are developed, with accelerations of the order of 10^5 times gravity[20]

APPARATUS

The apparatus available to us at the beginning of our investigation was designed by Mr Emerson Pray, then president of the Radio-Sonic Corporation, New Rochelle, N Y He had been engaged in ultrasonic investigation for many years and became interested in this possible application In Mr Pray's unit, the power output was variable from 0 to 1000 electrical watts, and the frequency range was variable from 100 to 1550 kilocycles per second

High voltage cable linked the generator to the transducer, which consisted of copper coil connected to a silver plated quartz crystal mounted in a ceramic and metal doughnut-shaped holder, supported in a heavy glass jar The natural period of vibration of this quartz crystal was 265 kilocycles per second The transducer was insulated by filling the jar with transformer oil so that the coil, holder and crystal were completely immersed An air bubble was placed beneath the crystal, thereby forcing the energy to leave the superior face of the crystal, through the circular opening in the holder

When the crystal in the apparatus was activated, the energy leaving the crystal caused a fountain of oil to rise in its path With the frequency between 100 and 500 kilocycles, the jet of oil droplets reached a height of 10 to 12 cm Approximately eighty per cent transfer of energy could be achieved when the object to be treated ultrasonically was placed in the oil fountain at an integral number of half wave lengths from the crystal. During activity, small bubbles of gas form in the center of the oil bath as a result of cavitation,[2] and intense heat is generated there. The output of the apparatus can be found with reasonable accuracy by the measurement of this heat or by the determination of the power used in the plate circuit of the oscillator.

A flat-bottomed flask of Pyrex glass, containing 20 cc of distilled water was suspended in the oil fountain above the crystal, at a depth at which satisfactory energy transfer was indicated, by the height of the water fountain created in the flask. A flask of Pyrex glass was chosen after it had been demonstrated that Pyrex glass is an excellent conductor of ultrasonic energy.* During ultrasonic activity, it was noted that the oil adhering to the outer surface of the flask formed ridges due to the presence of standing waves as the glass vibrated in resonance. The distance between two ridges of oil was the wave length being generated (from 2 to 4 mm.). The output was then adjusted to give 5 watts of sound power per square centimeter. This was chosen as the limit within which clinical application would be determined because many investigators had shown this power density to be nondestructive to tissue.[1, 9, 24, 25]

PROCEDURE AND OBSERVATIONS

Preliminary experiments. Calculi of nearly the same size and shape were selected from the collection of gallstones and urinary calculi available. With each stone, an attempt was first made to crush or crumble the stone by finger pressure exerted at all angles. As expected, some calculi were so dry that the outer layers did crumble away, leaving a hard core. The calyceal prongs on several of the staghorn calculi also crumbled away easily. A group of calculi which resisted crumbling were chosen for ultrasonic treatment (figs. 1, 2, 3; table 1).

Each calculus in turn was placed in the flask, immersed in distilled water and exposed to a power density of 5 watts/sq. cm. for intervals of 1, 2, 3 and 5 minutes. No gross changes were apparent in any of these stones, although the water was discolored and sediment was sometimes apparent. At the end of 1, 2 and 3 minute treatment intervals, the stones were tested by finger pressure and were found to be as resistant as before treatment. In most instances, however, the stones treated continuously for 5 minutes did crumble rather easily under finger pressure. The effect of variation in frequency range between 100 and 1500 kilocycles was then studied, using a barium titanate crystal for the higher frequencies. The higher the frequency, the longer the time interval during which the stone had to be treated before it could easily be crushed in the fingers; at 1500 kilo-

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* A number of tests demonstrated the capacity of Pyrex glass to conduct ultrasonic energy: A person holding one end of a Pyrex glass rod in the oil fountain was promptly aware of the heat generated by friction; an activated Pyrex rod was able to drill holes within ten minutes through plastic squares one-fourth inch thick; in a Pyrex test tube, a drop of mercury in 10 cc of water formed an emulsion that lasted six hours after the exposure to ultrasonic energy.

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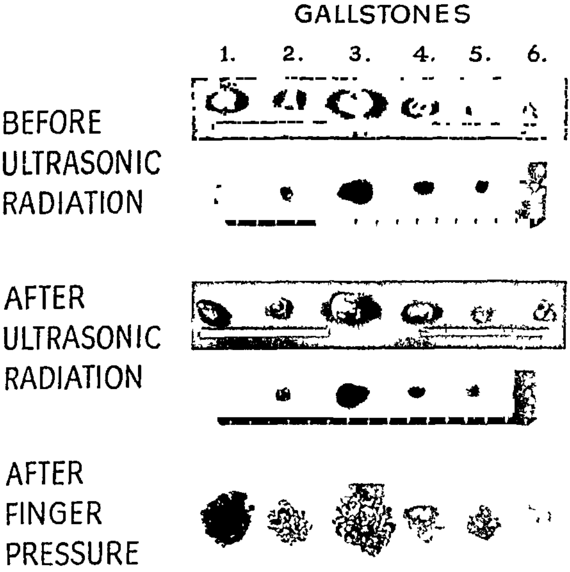

FIG 1

cycles the time required was 30 minutes Furthermore, the number of stones resisting crumbling was greater at the higher frequencies Apparently the size of the stone is not critical, at least up to the largest available to us, which was a bladder calculus approximately 4 inches in longest diameter Calculi with rough, irregular surfaces, however, seemed to be more resistant than the smooth surfaced stones After treating some fifty calculi in the manner described, it was determined that the best results were obtained by treatment for 5 minutes at a frequency of 350 kilocycles/second with a power density of 5 watts/sq cm

About twelve large calculi were then cut with a jeweler's saw into comparable pieces, and the open faces were sealed with Du Pont cement These were then treated under the optimum conditions indicated above Thin slices of the stones were examined both before and after ultrasonic treatment with a strong lens, some being placed under the microscope using a special substage light which could penetrate the structure We were able to obtain better preparations with the gallstones than with the urinary tract calculi Even in these crude preparations, however, it was possible to note, before ultrasonic treatment, the irregular, nondescript pattern of crystalline structure in some stones, and the regular ovoid rings, often of different density and color, in others Following exposure to ultrasonic energy, the particles seemed to be arranged in rows like military cadets on parade Between the rows the material seemed less dense, and here and there

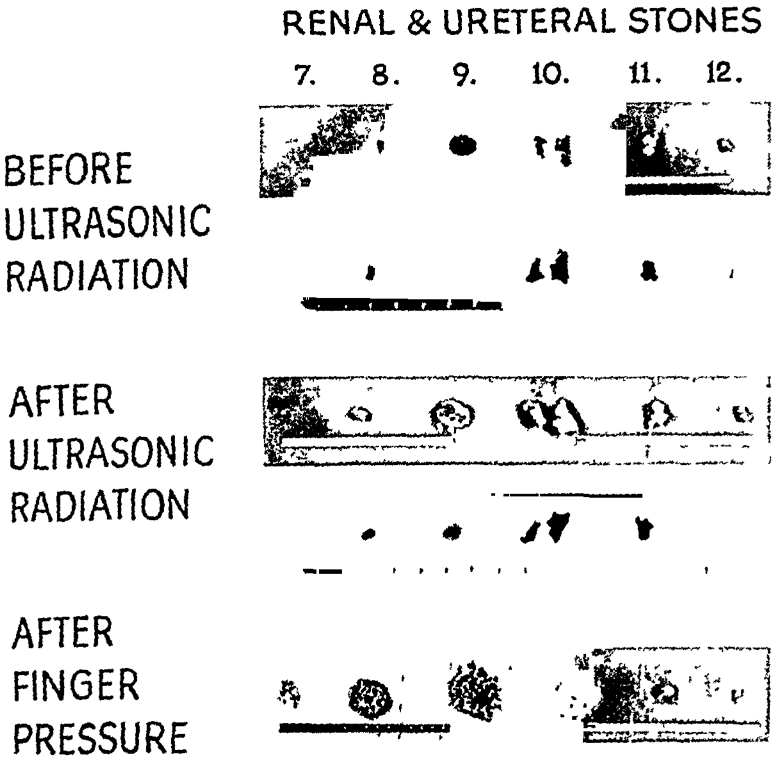

Fig. 2

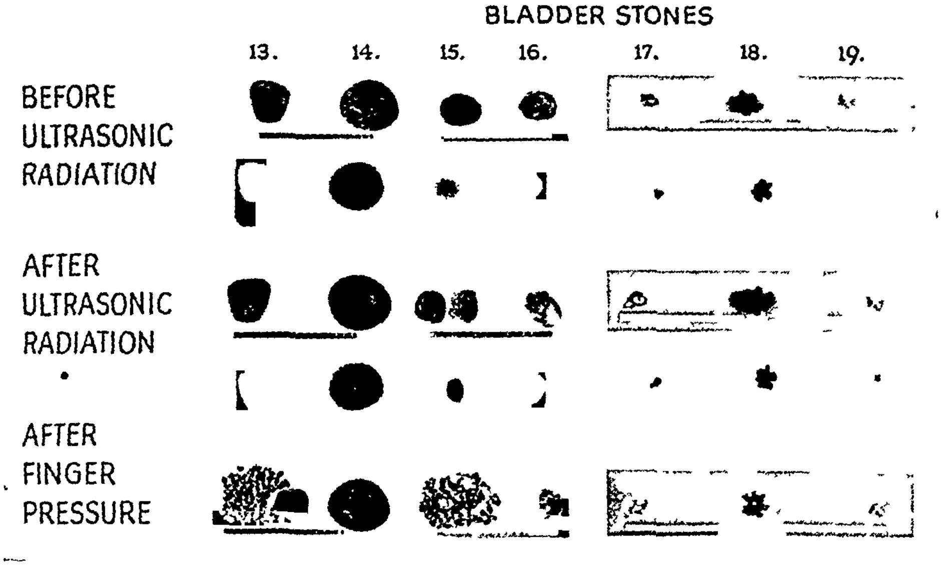

Fig. 3

were globules of translucent matter. We have surmised that these translucent areas represent water of crystallization expressed by the extreme stresses of the ultrasonic treatment.

It should be emphasized that the stones were not disintegrated by the ultra-

TABLE 1 *Chemical analyses*

Stones 1–6	Gallstones
Stone 7	White chalky outside, brown nucleus Outer layers Apatite { calcium carbonate calcium phosphate Some magnesium ammonium phosphate
Stone 8	White shaped like egg extremely hard outside, *chalky inside* Outer layers Calcium carbonate Calcium phosphate Magnesium ammonium phosphate Trace of urate Inside Calcium carbonate Calcium phosphate Ammonium urate
Stone 9	Calcium carbonate Calcium phosphate Magnesium ammonium phosphate Urate
Stone 10	45 gm—extremely hard—plasterlike in appearance Calcium phosphate Calcium carbonate Magnesium ammonium phosphate
Stone 11	Calcium phosphate
Stone 12	Calcium carbonate Calcium phosphate Ammonium phosphate
Stone 13	Calcium carbonate Calcium phosphate Magnesium ammonium phosphate Urate
Stone 14	*White crystalline* Calcium carbonate Calcium phosphate
Stone 15	White outside—dark brown inside Chiefly Calcium oxalate with some calcium phosphate
Stone 16	Tan outside—dark brown inside Calcium oxalate Calcium phosphate
Stone 17	Calcium phosphate Calcium carbonate Magnesium ammonium phosphate *Trace of calcium oxalate*
Stone 18	Dark brown—15 5 gm Chiefly calcium oxalate Trace of calcium phosphate
Stone 19	Tan outside—dark brown inside Calcium oxalate

some energy alone, as we had hoped, but that some additional physical force was always required It appeared, moreover, that the finger pressure had to be exerted in a direction parallel to the rows of crystalline structure in order to crumble the stone A definite change, however, did occur in most of the calculi, both biliary and urinary, when they were exposed for five minutes to a sound power of 5 watts/sq cm

Experiments on living tissue The foregoing experiments were demonstrated by Mr Pray and the author at the May 1950 convention of the New York State Medical Society At about the same time, Lamport, Newman and Eichorn[26] reported on related studies they had been conducting in animals They had treated gallstones in an exteriorized loop of intestine with ultrasonic energy and had succeeded, in 80 per cent of their trials, in breaking up the stones. We felt encouraged, therefore, to extend our experiments to a study of ultrasonic effects on living tissue.

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[26] Lamport, H, Newman, H F and Eichorn, R D *Fragmentation of biliary calculi* by ultrasound Fed Proc, 9 73, 1950

While awaiting the construction of a proper mobile transducer, wherein various barium titanate crystals could be mounted, we treated some operative specimens ultrasonically to determine the extent of tissue damage. A kidney was obtained immediately after its removal from a patient with calculous pyelonephritis. The specimen was placed in a flat-bottomed Pyrex beaker and covered with distilled water. The beaker was then suspended in the oil fountain at a depth at which adequate energy transfer was assured. The central beam of energy was impressed into the large stone in the pelvis, but the entire kidney was exposed to the ultrasonic energy. Treatment was carried out for five minutes at a power density of 5 watts/sq. cm. When the treatment was terminated, temperature of the water was found to have risen to 65°C, and the kidney surface was somewhat blanched. Upon section, no gross changes were apparent, except those usually seen with calculous pyelonephritis. The contained calculus was soft and easily fragmented, but we do not know how resistant it may have been before treatment. The pathologist later reported that, because of the extensive infection present, any evaluation of the effects of ultrasonic treatment was impossible. In any case, no evidence of extensive tissue destruction by heat or ruptured cell walls was noted. The same experiment repeated on two other specimens yielded no new knowledge.

Another kidney specimen, secured in the same manner, was sectioned into four segments and exposed to varying densities of sound power.

Segment one	at 2.5 watts/sq.cm.	for 5 minutes
Segment two	at 2.5 watts/sq.cm.	for 10 minutes
Segment three	at 18 watts/sq.cm.	for 1 minute
Segment four	at 18 watts/sq.cm.	for 2 minutes

Examination of these exposed segments revealed no gross changes except for a grayish blanched appearance of the third and fourth segments. In the third and fourth specimens too, the water temperature was found to have risen to 78°C. The pathologist again reported that tissue changes incident to infection made it impossible to evaluate any change due to ultrasonic treatment, but areas of necrosis were noted in segments three and four which were not present in the other sections.

The tails of three white rats were then exposed to a power density of 5 watts/sq.cm. for 5 minutes. The rats were obviously uncomfortable under the treatment, but no tissue destruction occurred during a 48-hour observation period. Each rat was then suspended in such fashion as to allow the tip of the oil fountain to contact the lower abdomen of the animal. The rats were again subjected to a power density of 5 watts/sq.cm. for 5 minutes. All died within 48 hours. Autopsy revealed peritonitis due to rupture of the intestine, but damage to the superficial tissue was minimal.

One trial was made with the mobile hand-held transducer applied over the lower abdomen of a white rat It was impossible to make close contact with the animal, and the energy transfer was almost nil Difficulty was also encountered with the oil circulation needed to cool the crystal

Experiments with a focused crystal In the mobile transducer, a focused barium titanate crystal with a frequency of 1500 kilocycles was mounted The crystal was 1 5 cm in diameter, and with 75 watts of electrical energy delivered to the crystal, it was estimated that the sound power density was 8 watts/sq cm for a 5 minute treatment period The apparatus was set in a tank of water so that circulating oil was not necessary to cool the crystal, and the beam of energy was directed along the length of the tank A trolley with a wooden clothespin holder was devised by which the calculus could be treated at different distances from the crystal From the wave disturbances in the tank of water, it was possible to determine fairly accurately the locations of the nodes present The stones were then placed at these nodes The focal point was determined to be 16 cm and at this point the calculi were softened so that they crumbled easily in the fingers At all other points, however, such softening did not occur, although, theoretically, standing waves should make other points just as active A large bladder calculus of calcium carbonate, 4 by 1 5 cm, was treated in the same manner Ten minutes of treatment were necessary to soften this stone

DISCUSSION

Further experiments and consultations with Dr Harold Beyer, of the Sloan-Kettering Institute, and Dr Ivan Greenwood, of the General Precision Laboratories, led to the conclusion that the amount of sound power necessary to produce significant changes in calculi is so great that severe damage to the intervening tissue is certain in any clinical procedure in which ultrasonic energy is applied at the body surface in order to affect stones in the kidney or the bladder

Pohlman's work[1] on tissue absorption also indicates that adequate energy to affect a bladder or renal calculus in situ would be very destructive to tissues in the path of the energy Pohlman found that at 800 kilocycles, the half-value layer, or the depth at which the radiated intensity has decreased to half its incoming value, was 4 9 cm in fat muscle tissue When the frequency was increased to 2400 kilocycles, the half-value layer was reduced to 1 5 cm Deep penetration of tissue thus depends on reducing the frequency or increasing the intensity The latter factor increases tissue damage as well as the strain on the crystal, this added strain on the crystal may cause it to fracture By decreasing the frequency, the wave length is increased with a resultant loss of resolving power and a widening of the ultrasonic beam This would probably result in in greater tissue damage over a wide area, while the power density brought to bear upon a bladder calculus at an estimated depth of 6 cm would be negligible

The possibility of a direct application of ultrasonic energy to a bladder calculus through an instrument like the cystoscope has been presented to American Cystoscope Makers, Inc The problems connected with maintaining contact between the calculus and the crystal have been explored with Mr Frederick J Wallace and Dr Charles Spaeth Investigations along these lines are continuing

Mulvaney[27] reports on "button" type applicators, while Lamport and Newman[28] report on "ultrasonic drilling" of ureteral calculi in cadaver experiments.

SUMMARY AND CONCLUSION

The effects of ultrasonic energy on calculi which form in the human body, specifically urinary tract and gallbladder calculi, have been investigated.

Apparatus is now available for controlled experimentation using electron tube oscillators of varying frequencies as generators and quartz or ceramic piezoelectric crystals of varying frequencies and shapes as transducers. An oil or water coupling is necessary between transducer head and work in order to achieve efficient transfer of energy, since ultrasonic waves will not progress through air.

By the proper application of ultrasonic energy to urinary and biliary calculi, changes tending toward disintegration have been achieved in the majority of instances. These changes appear to consist of a rearrangement of particle constituents so that the calculus is more easily crumbled than before treatment. All stones, however, were not equally affected, and a few were actually resistant to change, within the limits of our equipment. The lower frequencies from 250 to 500 kilocycles, with a power density of 3.5 to 5 watts/sq. cm. and an exposure time of 5 minutes, gave the best results in situ.

Ultrasonic treatment of calculi by the application of the energy source at the surface of the body seems impractical because, even with a focused crystal, the power required to penetrate from the surface to the calculus-containing organs and to impress an adequate power dosage on the stone would certainly be lethal to intervening tissues and organs.

The application of this modality through an instrument like a cystoscope requires a small, rugged crystal as the energy source. This is not presently available. It is hoped that further experimentation will overcome this and other problems in the application of ultrasonic energy to urinary and biliary calculi in the body.

Deep appreciation due Mr. H. H. F., who prefers to remain anonymous but whose scientific interest and financial support have assured future work in this project, and to Dr. Victor F. Marshall, of the New York Hospital-Cornell Center, for his constant stimulation.

140 East 54th St., New York 22, N. Y.

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[27] Mulvaney, W. P.: Attempted disintegration of calculi by ultrasonic vibrations. J. Urol., **70:** 704, 1953.

[28] Lamport, H. and Newman, H. F.: Critical appraisal of methods for disruption and extraction of urinary calculi, especially with ultrasound. Yale J. Biol. & Med., **27:** 395, 1955.

THE JOURNAL OF UROLOGY
Vol 75 No 5 May 1956
Printed in U S A

A MODIFIED CATHETER FOR THE DRAINAGE OF CUTANEOUS URETEROSTOMY

GEORGE J BULKLEY

Management of the patient with cutaneous ureterostomy is often complicated by the tendency of stenosis to occur at the stoma This frequently requires an indwelling catheter for collection of urine and maintainance of an adequate skin opening The catheter in the ureter is also apt to cause complications due to infection, leakage and alkaline encrustation or stone formation

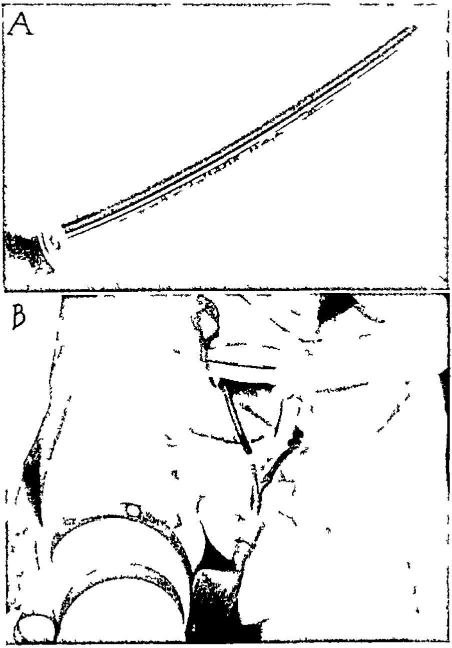

FIG 1

During the past few years we have had under our care a patient upon whom we performed a total cystectomy and bilateral cutaneous ureterostomy Drainage of the ureters by catheter was never satisfactory because of leakage of urine around even a large catheter and because of recurrent encrustation and stone formation on the catheters in spite of careful management Drainage by the

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Read at annual meeting of North Central Section of American Urological Association, Chicago, Ill September 29 October 1, 1955

Singer cup cemented to the skin was accompanied by persistent stenosis of the ureteral opening requiring dilatation at weekly intervals to maintain adequate drainage.

To combine the advantages of a short indwelling catheter for maintaining an adequate skin opening with a water-tight cemented skin cup, we devised a polyvinyl catheter with a flange (fig. 1, *A*). The flange is approximately 1½ cm. in diameter and is welded onto the end of a polyvinyl catheter 12 to 18F. The catheter is cut to desired length, usually 2 to 4 inches, in order to prevent stricture formation of the distal ureter. The catheter is introduced into the ureter so that the flange is flush with the skin and the cup then cemented to the skin around the flange in the usual manner (fig. 1, *B*). When the cup is changed, the catheter is removed and cleaned.

This method has now been used more than 2 years by our patient and has proved far superior to all methods previously tried. The apparatus is changed at intervals of about two weeks and is handled entirely by the patient without difficulty or complications.

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A SIMPLIFIED BLADDER SCOOP

JOSEPH H LIPTON

From the Urologic Service, Lynn and Union Hospitals, Lynn, Mass

Most urologists frequently have wished for a simple instrument to retrieve a biopsy, a small calculus or an elusive piece of resected prostate from the bladder Existing flexible rongeurs and small lithotrites have sometimes proven difficult to manipulate On occasion, attempts to grasp a pea-sized stone spread the jaws of the instrument sufficiently to traumatize the urethra on withdrawal Furthermore, adequate visualization is sometimes difficult, especially with the lithotrite

The following simple instrument has been devised to insure easy removal of the aforementioned specimens Using an ordinary resectoscope electrode as a model, the cutting loop has been replaced by a stainless steel scoop, and the arms leading from the scoop considerably strengthened The resultant "scoop" has exactly the same dimensions, in order that it may easily be substituted in the resectoscope working element, and it engages the specimen very simply and draws it into the sheath, withdrawing the working element brings the specimen smoothly out through the sheath The foroblique telescope affords the same unimpaired vision as is present during prostatic resection and this in itself is of tremendous advantage

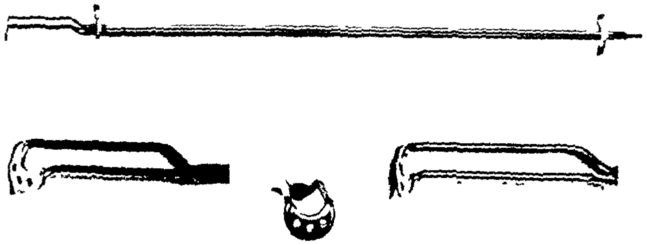

FIG 1

I have used this scoop repeatedly for removing resected portions of bladder tumor, for various calculi up to the size of a pea, retained bits of prostatic tissue, and fragments of calculi after crushing with other instruments Its smooth edge has also been very satisfactory in removing adherent slough or fibrinous material

I am indebted to C R Bard Inc and the Greenwald Company for following my design in the manufacture of this instrument A modification is being prepared in which the scoop is curved inward at the lower edge enabling a better engaging effect Figure 1 shows the entire scoop and enlargements of the head from different angles

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THE JOURNAL OF UROLOGY
Vol. 75, No. 5, May 1956
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A NEW TIMBERLAKE OBTURATOR ATTACHMENT FOR PASSAGE OF RESECTOSCOPE UNDER ADVERSE CONDITIONS

SIDNEY P. HURWITZ AND EDWARD B. JACOBSON

Urethral dilatation prior to transurethral surgery is usually an uneventful procedure. Occasionally, one encounters an obstruction to the passage of the van Buren sound due to a false passage, stricture, fold of mucosa, or an unusually large prostatic median lobe. Further manipulation in attempting to bypass the obstruction often leads to undue trauma to the urethral mucosa and corpus spongiosum with associated chills and fever.

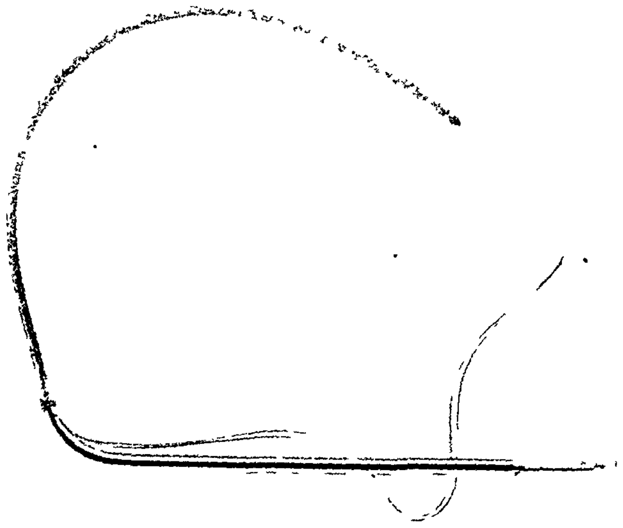

FIG. 1

If the obstruction becomes nonpassable, one must resort to perineal urethrotomy or suprapubic surgery. This necessitates an explanation to the patient, who psychologically has been prepared for an uneventful procedure.

In order to overcome this occasional complication we have developed a new technique for urethral dilatation, and have devised an attachment for the Timberlake obturator which allows for the easy passage of the resectoscope sheath.

The technique is as follows:

Should the slightest obstruction be encountered along the course of the urethra, the sound is immediately removed and a No. 14 or 16 straight rubber catheter passed into the bladder. Regular van Buren sounds are then forcibly fitted into the flared end of the catheter and passed into the bladder, the catheter acting similar to a filiform guide (fig. 1).

Increasing caliber sounds are then passed up to a 30F or 32F—the catheter always remaining fixed to the sound. As a precautionary measure, a silk suture

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Read at annual meeting of North Central Section of American Urological Association, Chicago, Ill. September 29-October 1, 1955 may be attached to the end of the catheter for its withdrawal in case of accidental detachment.

After dilatation of the urethra is accomplished, the flared end of the catheter is cut off and its lumen fitted on to the new Timberlake attachment (figs. 2 and 3).

The resectoscope sheath is now ready to be introduced, again using the catheter as a *filiform guide*. Once the sheath is in place, the obturator with the attached catheter is easily removed from the lumen of the sheath.

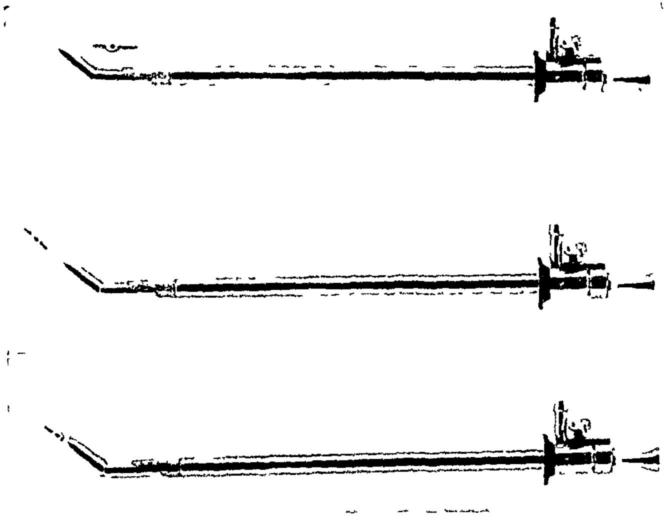

Fig 2

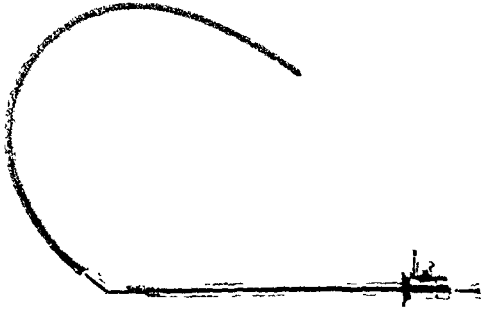

Fig. 3

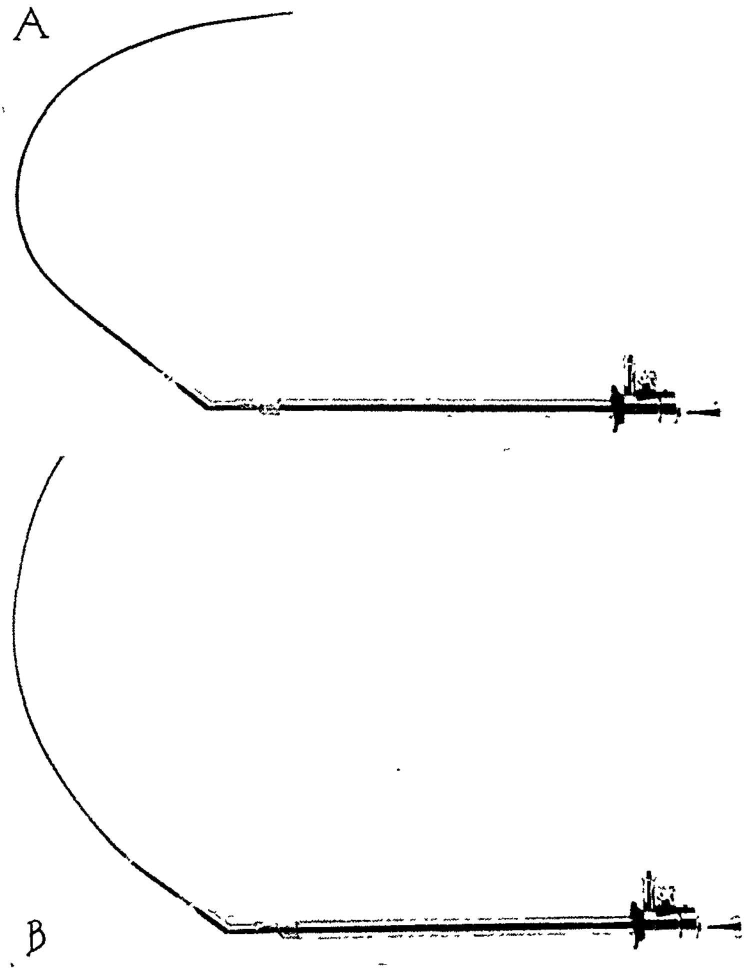

FIG. 4

This new attachment has been primarily designed for use along with the "catheter-sound dilatation technique." If one is unable to pass a catheter, but can introduce a filiform, dilatation may be carried out with Le Fort sounds. Female filiforms will fit the attachment (fig. 4, A), whereas male filiforms will fit directly into the tip of the obturator (fig. 4, *B*).

With the use of this technique and new removable Timberlake obturator attachment, we have overcome unnecessary trauma to the urethra and reduced the incidence of perineal urethrotomy and suprapubic intervention in our practice.

CONCLUSION

A new technique for urethral dilatation, and a new removable attachment for the Timberlake obturator which allows for the easy passage of the resectoscope sheath under adverse conditions have been presented.

We are grateful to Mr. Stephenson of the Greenwald Co., Gary, Indiana for his co-operation in fabricating the new attachment.

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Note by editor A complete list of the executive committees of the various sections, and a complete list of the officers and members of the executive committees of the various branch societies were printed in the December 1955 issue

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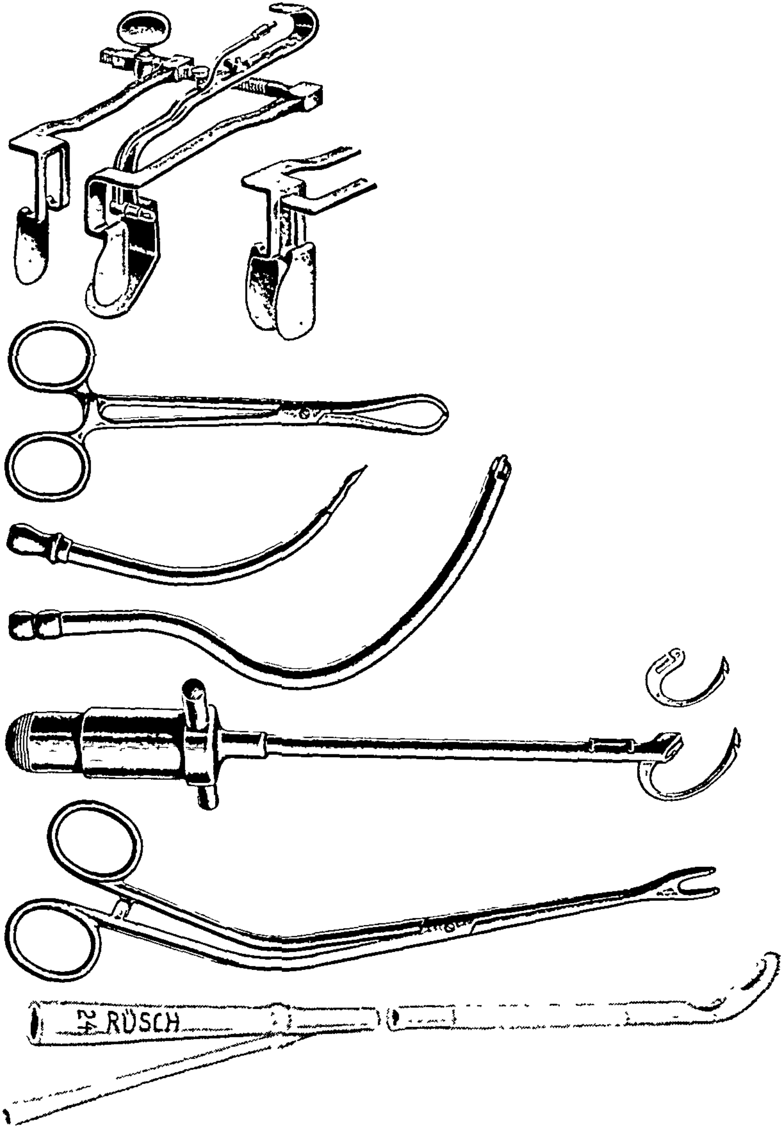

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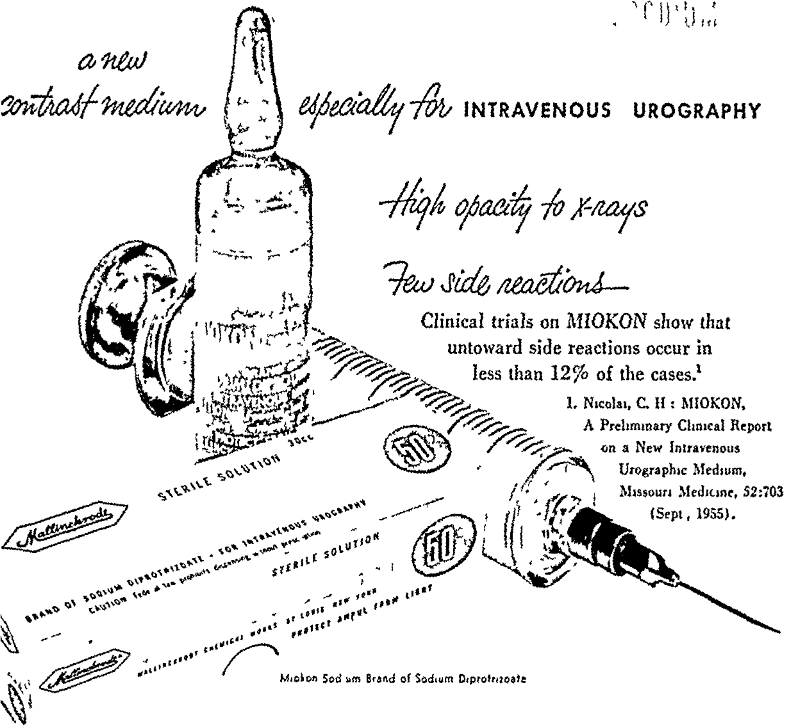
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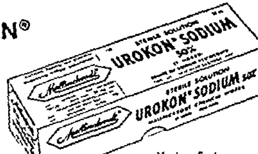

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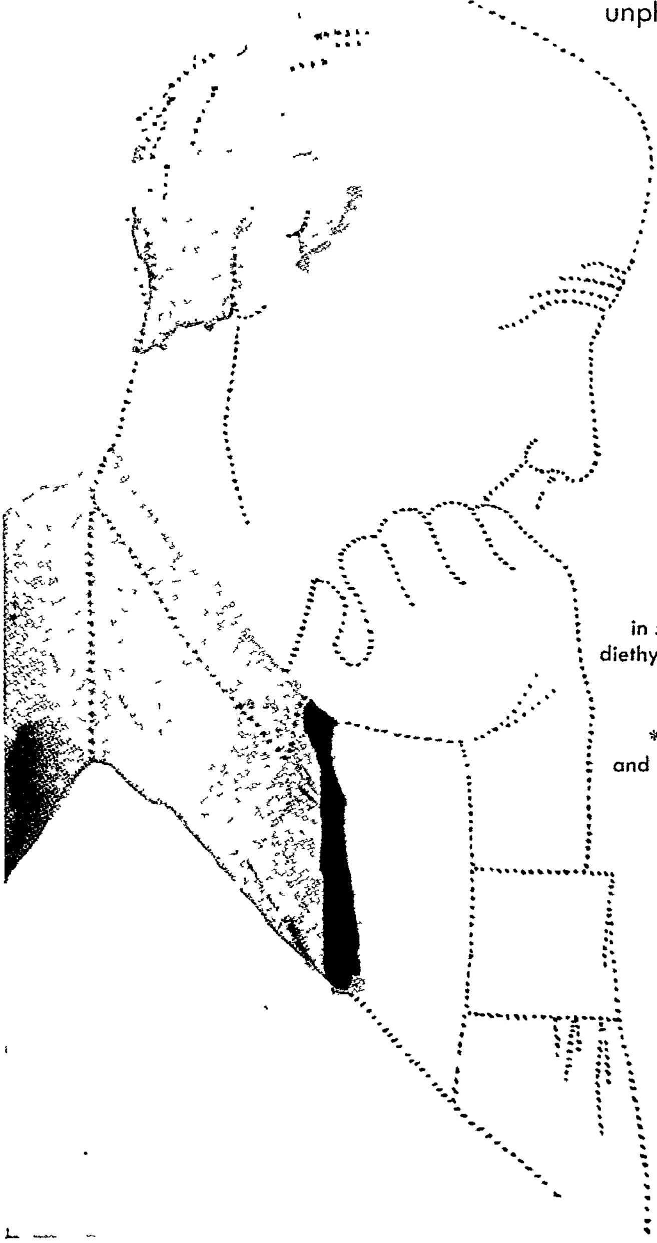

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[1] O'Conor, Vincent J.; Clorpactin WCS-90 in the treatment of interstitial cystitis. *Quarterly Bulletin* Northwestern Univ. Med. School, Chic., 1955, Vol. 29, No. 4, Page 392, Winter Quarter.

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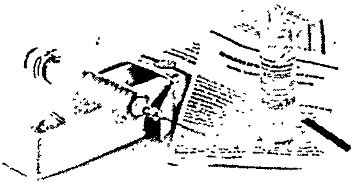

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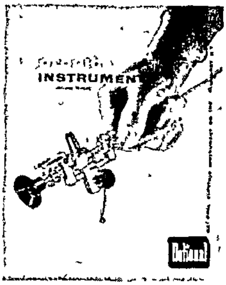

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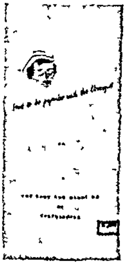

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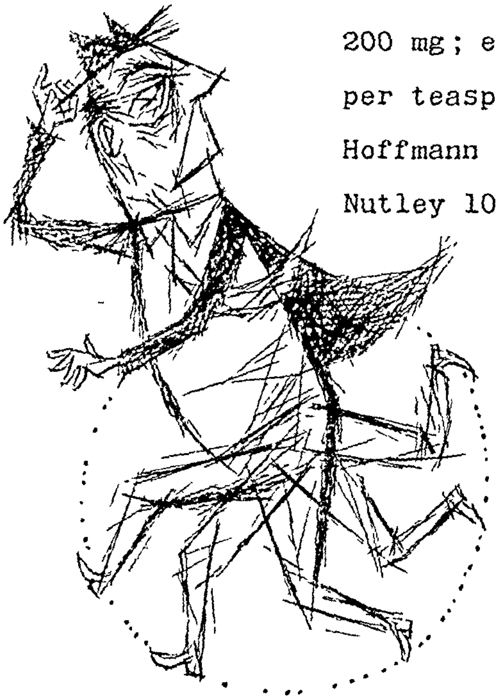

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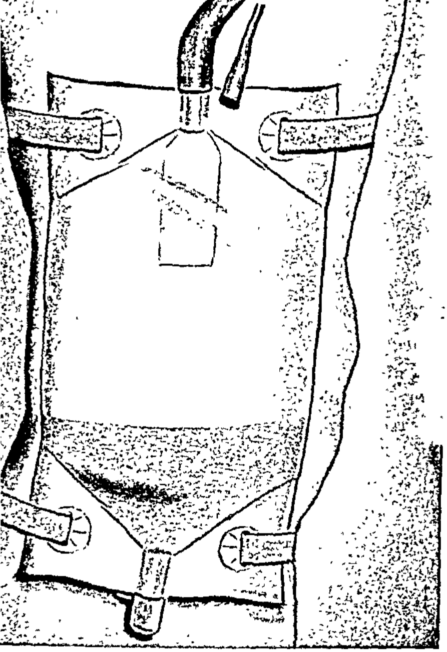

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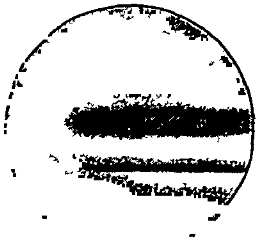

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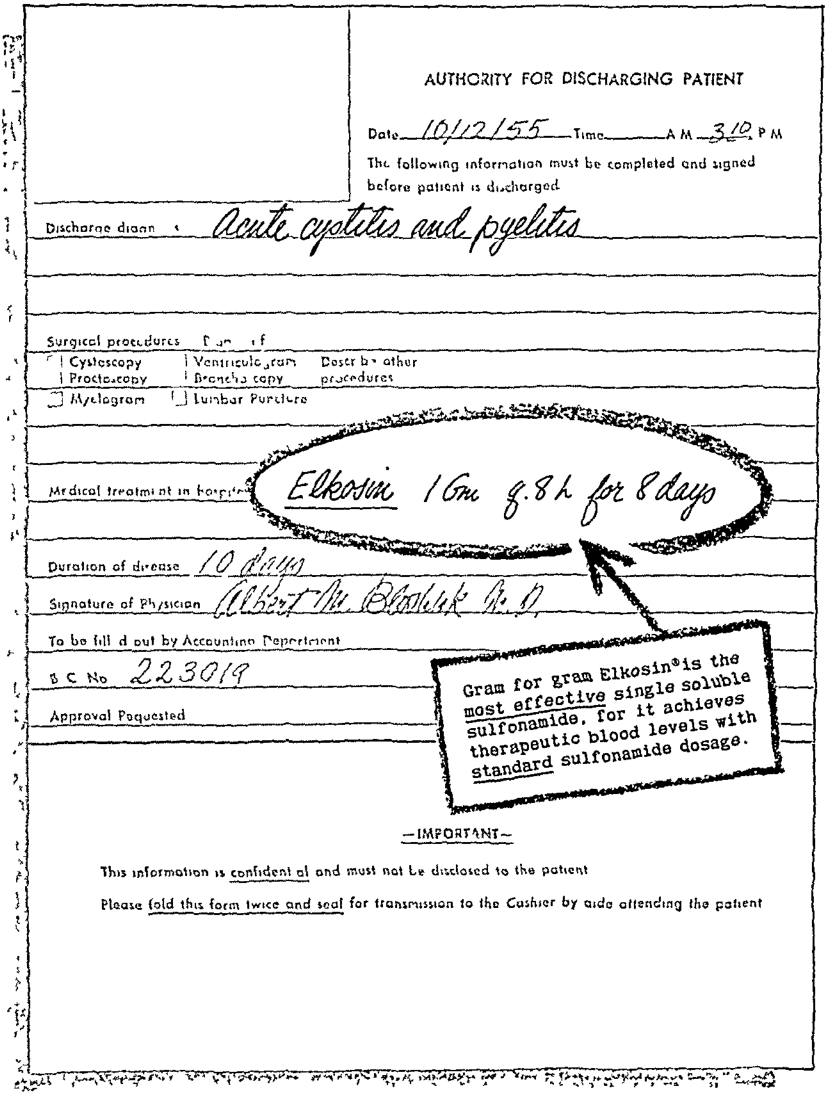

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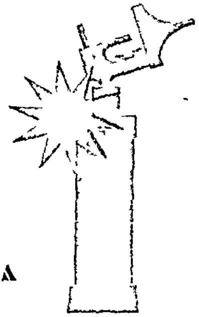

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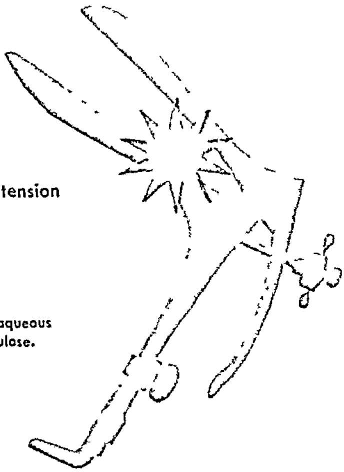

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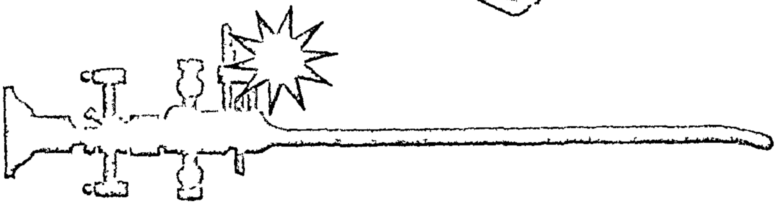

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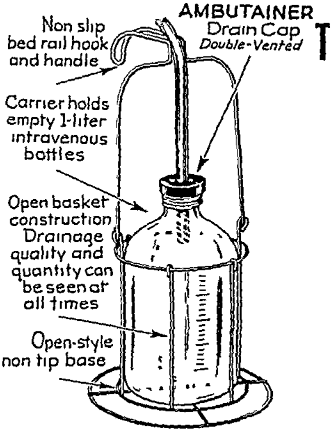

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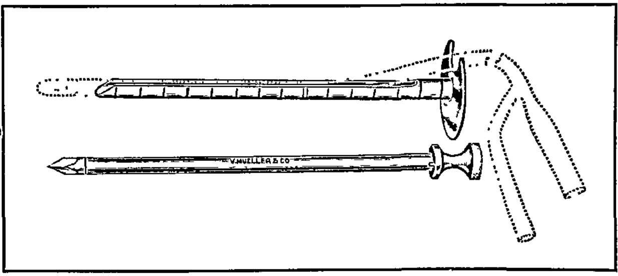

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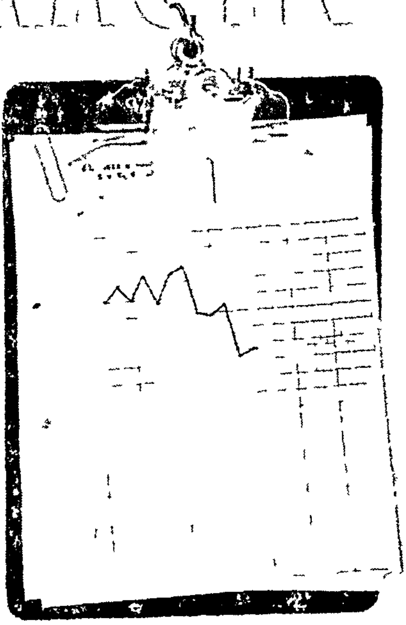

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CONTENTS

Basic Aspects of Radiation Therapy *W S Moos* 881
Antimicrobial Agents for Urinary Infections *R D Herrold* 892
Resection of Solitary Kidney *Meredith Campbell* 900
Simple Renal Cysts in Children *J H DeWeerd and H B Simon* 912
Differential Diagnosis Between Cancer and Solitary Serous Renal Cyst *B G Clarke W J Grade Jr H L Rudy and Lawrence Rockwood* 922
Disseminated Fatal Postpartum Candidiasis with Renal Suppuration *J B Davis J D Whitaker L K Ding and J H Kiefer* 930
Renal Functional Pattern in Calculous Disease *Alejandro Chait* 937
Electron Microscopy of Cystine Urolith *J H L Watson* 940
Experiences with Ileal Conduit in Urinary Diversion *W J Baker and E C Graf* 950
Urinary Incontinence in Leriche Syndrome *A M Tocker and W G Cauble* 961
Secondary Malignant Tumors of Bladder *E J Ganem and J T Batal* 965
Undescended Testes *J R Hand* 973
Rebound Phenomenon in Treatment of Spermatogenic Dysfunction *J H McDonald and N J Heckel* 990
Artificial Insemination with Testicular Tissue *G S Slater* 993
Urethrocystography in Differential Diagnosis of Prostatic Cancer *K J Oravisto and S Schauman* 995
Radical Perineal Prostatectomy *E A Webb and B A Smith* 1000
Hypothermia Induced by Cystoscopy *S I Roland* 1006
Reactions Due to Intravenous Urokon *V H Youngblood J O Williams and Allan Tuggle* 1011
Effect of Benadryl in Allaying Allergic Effects of Urokon *Jack Lapides and R E Boyd* 1016
Simple Method of Retaining Catheters *A E Comarr and T Torjerson* 1019
Maintenance of Sterility of Drainage Tubes *W E Forsythe, P J Stueber, Jr and M H Hamilton R N* 1023
Modification of McCarthy Cystoscope *J H Kiefer* 1025
Simple Cystoscopic Illuminator *Ben Seid and B E Cohler* 1027
Index 1029
Table of Contents Volume 75 iii

Annual Meeting, American Urological Association, Hotel William Penn
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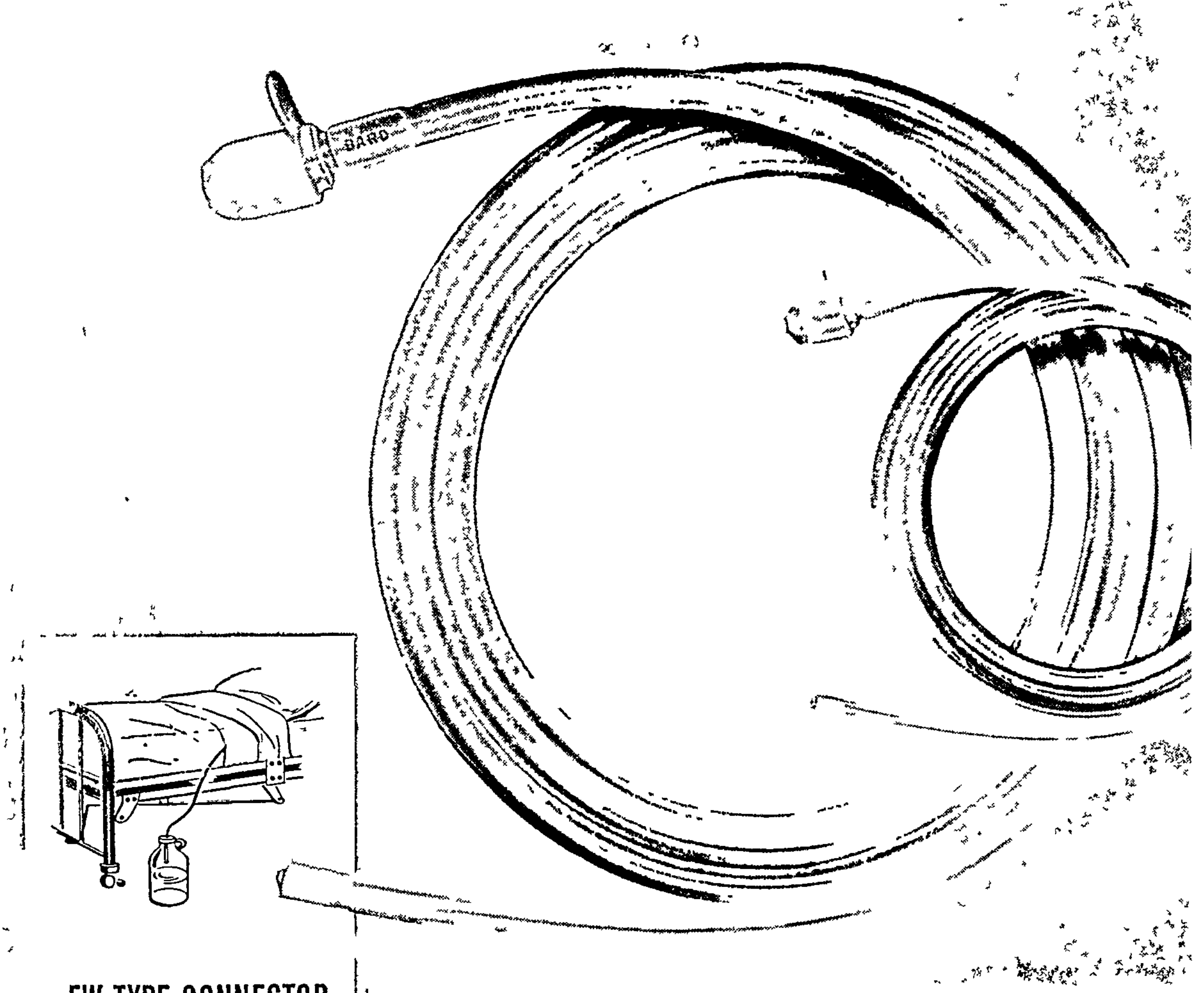

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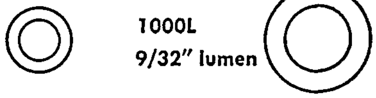

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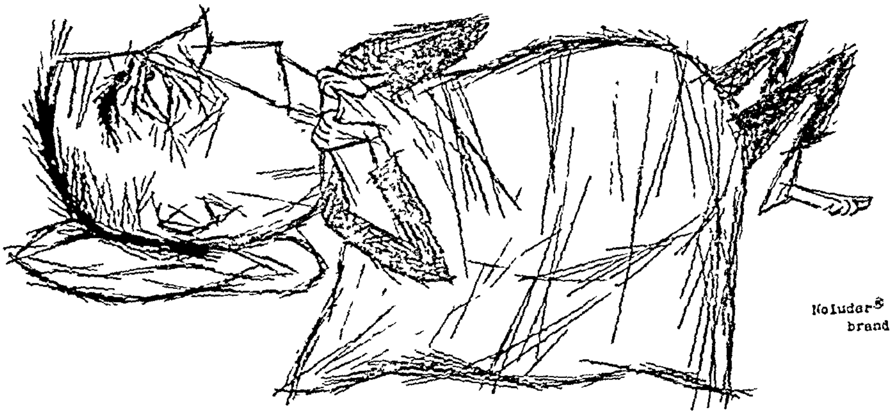

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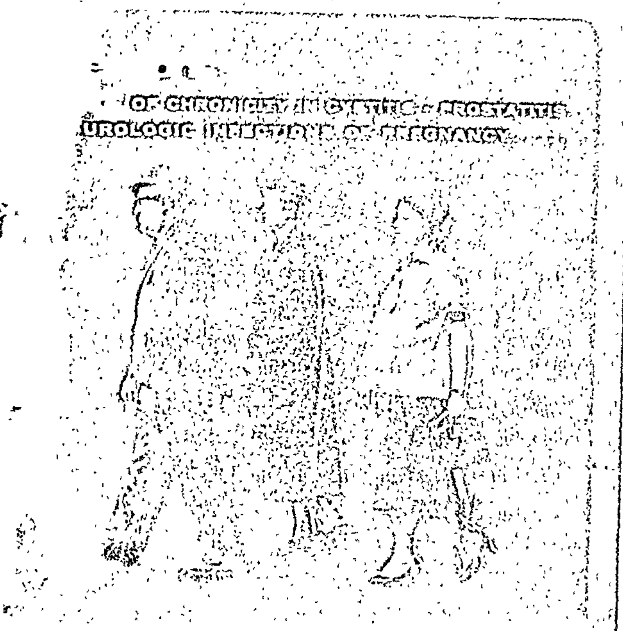

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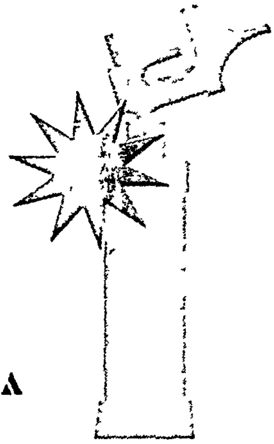

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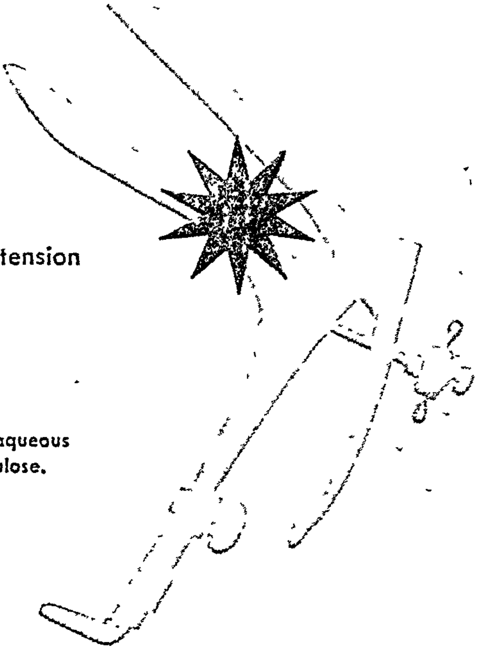

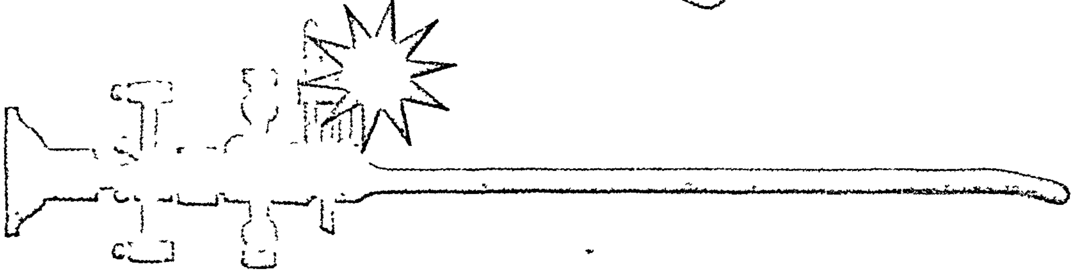

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REFERENCES 1 South M J 31 233 1938 2 J Urol 51 137 1944 3 Minnesota Med 33 103 1950

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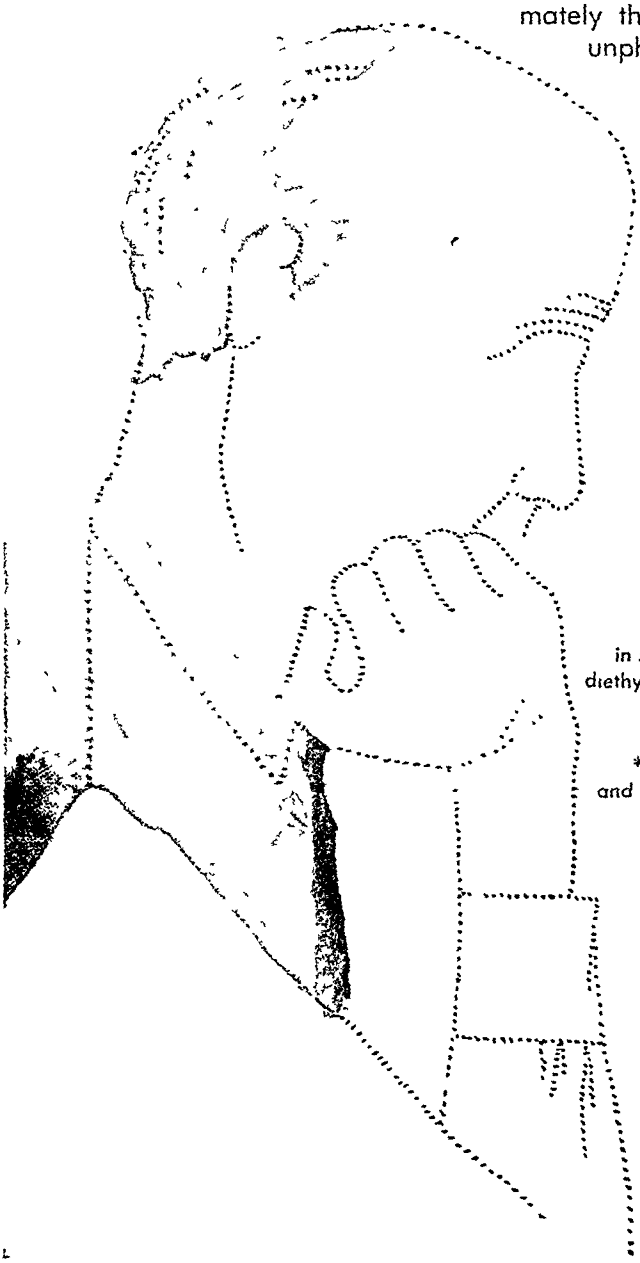

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*Flocks, R. H.; Marberger, H.; Begley, B. J., and Prendergast, L. J.: J. Urol. *74*:549, 1955.

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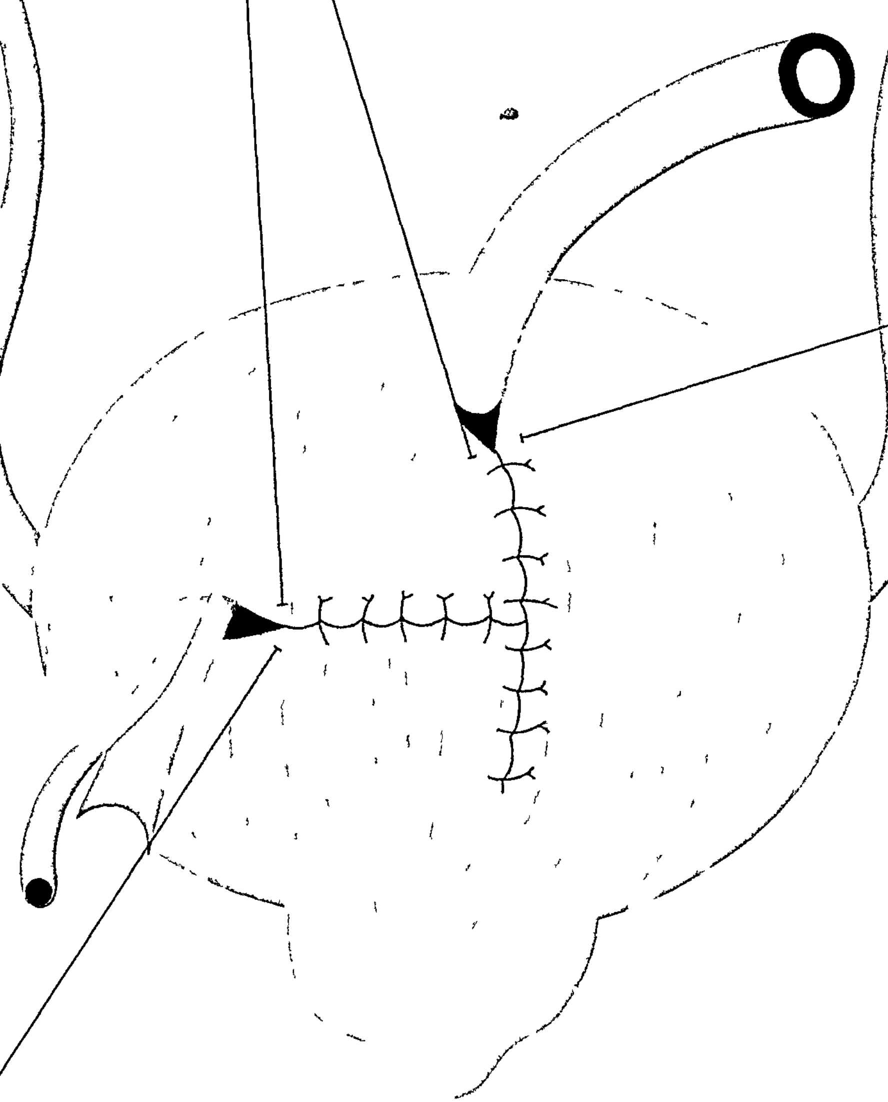

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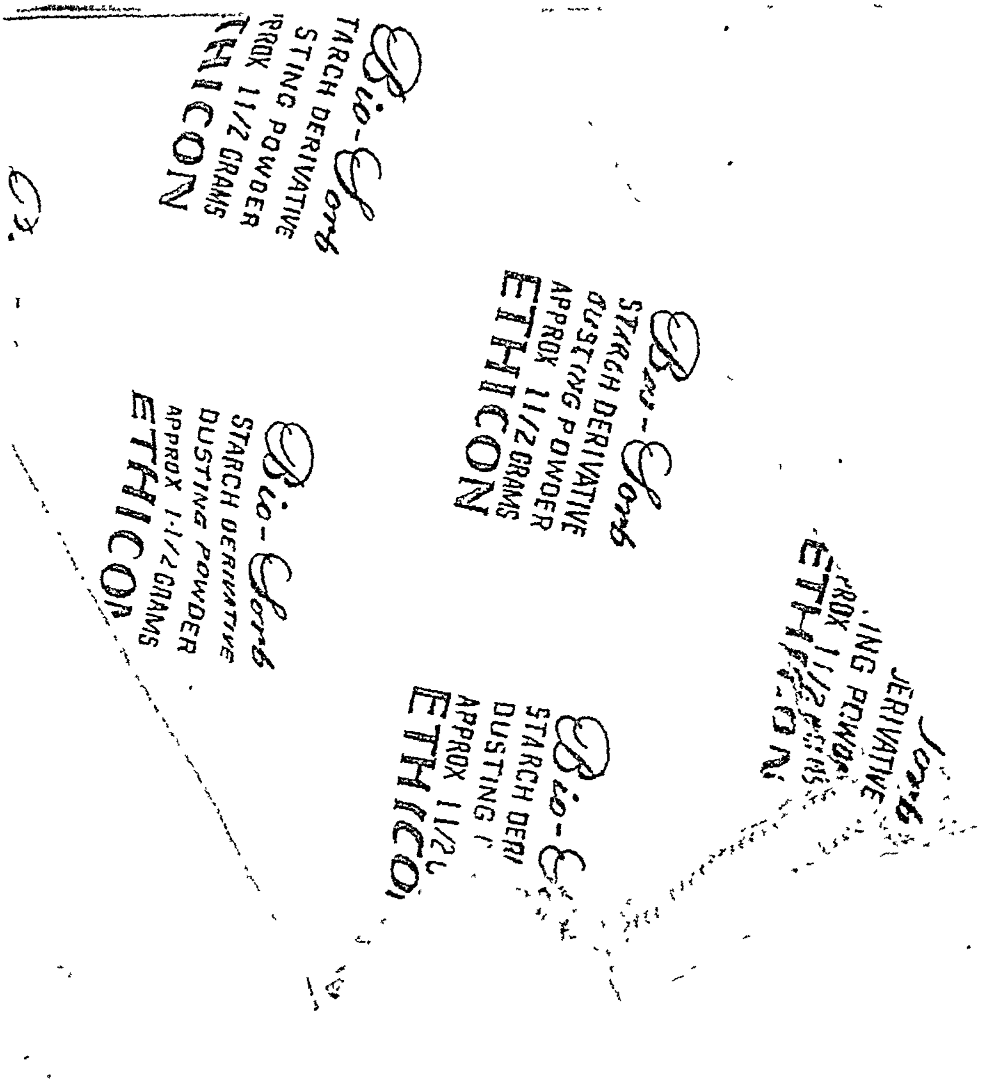

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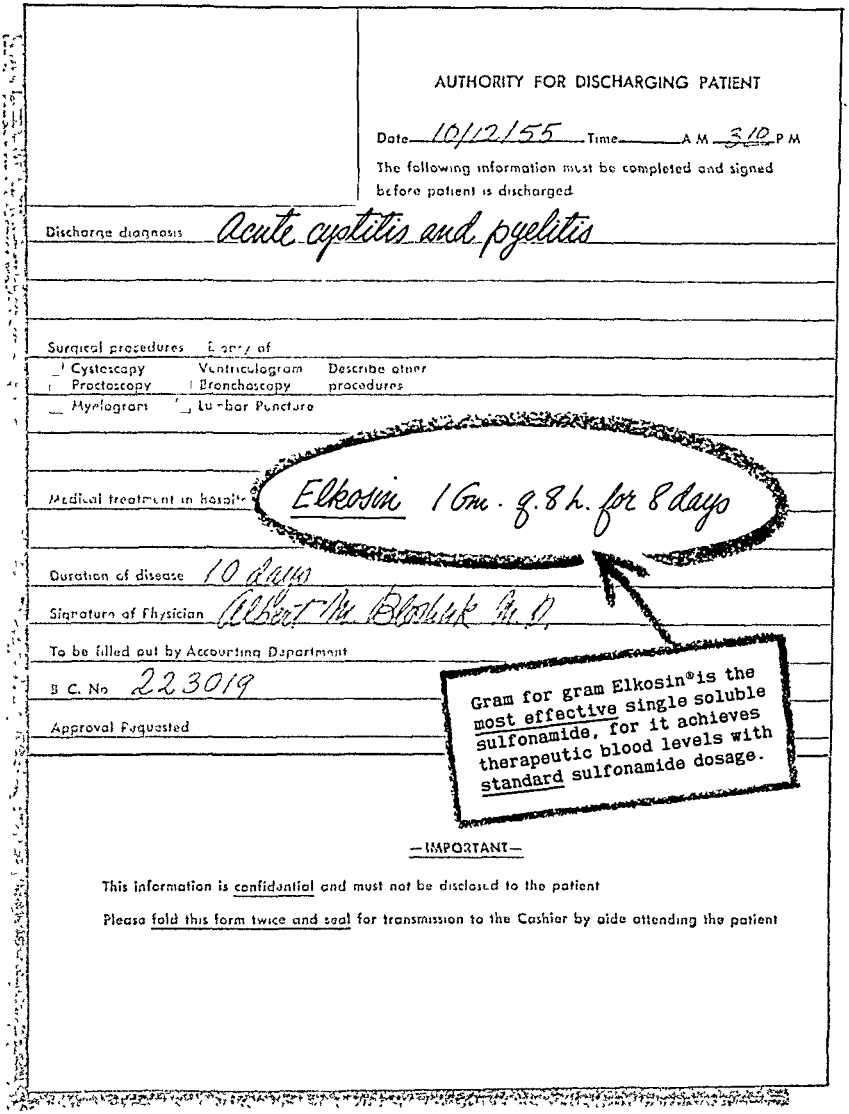

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Discharge diagnosis Acute cystitis and pyelitis

Surgical procedures [illegible] of

☐ Cystoscopy ☐ Ventriculogram Describe other procedures

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Medical treatment in hospital Elkosin 1 Gm. q.8 h. for 8 days

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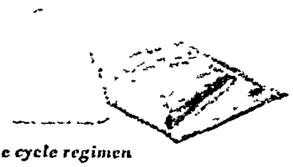
*Personal Communications to Medical Department, Eaton Laboratories. Detailed information available on request



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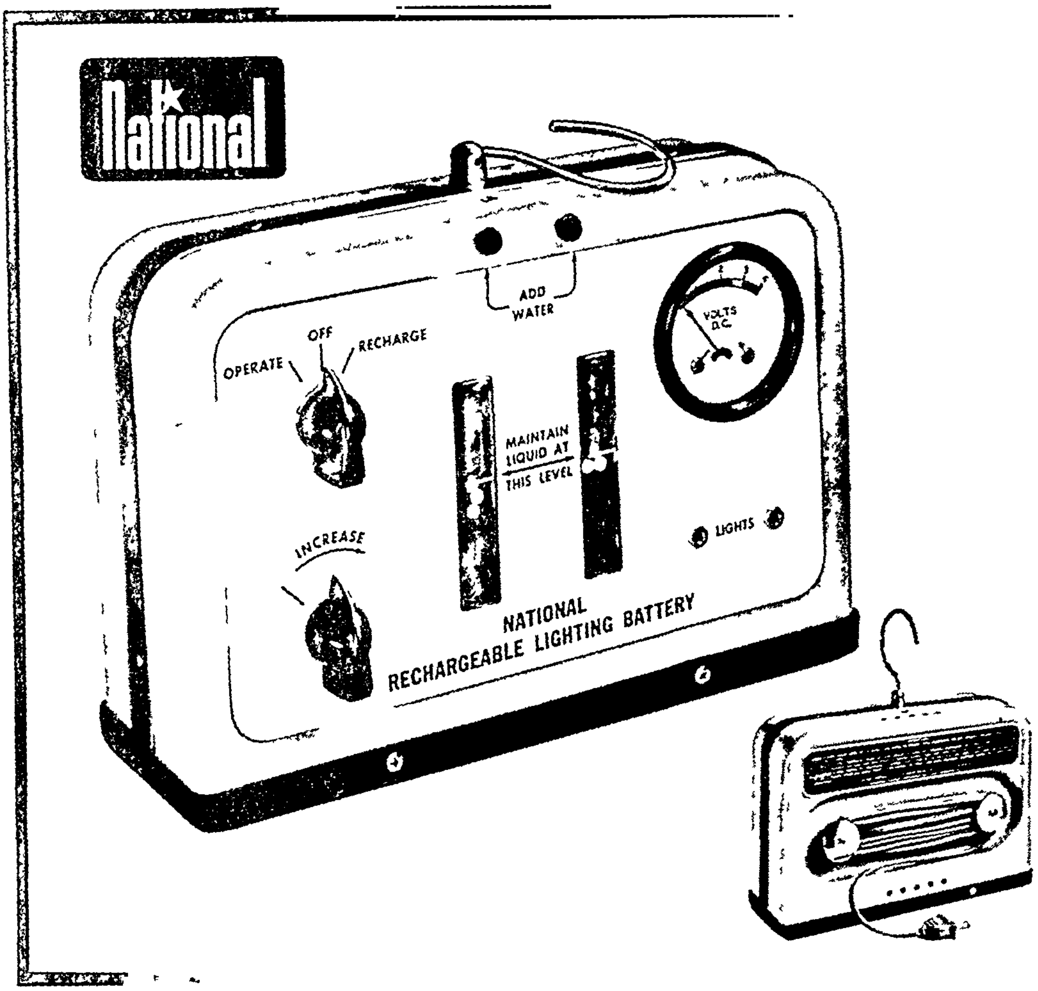
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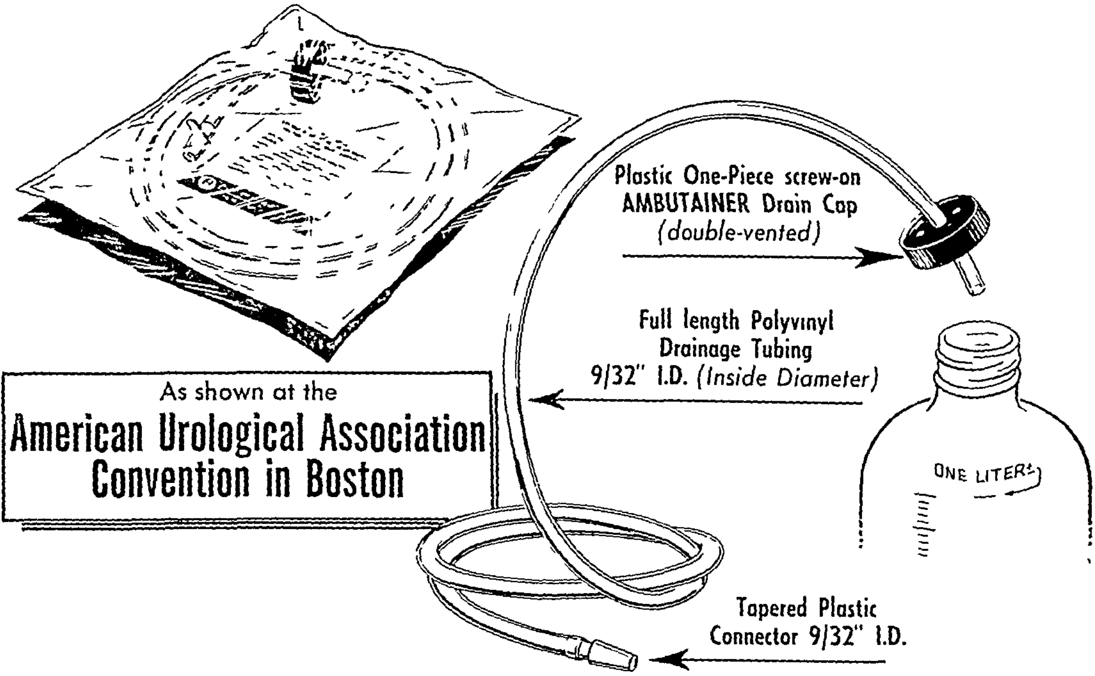

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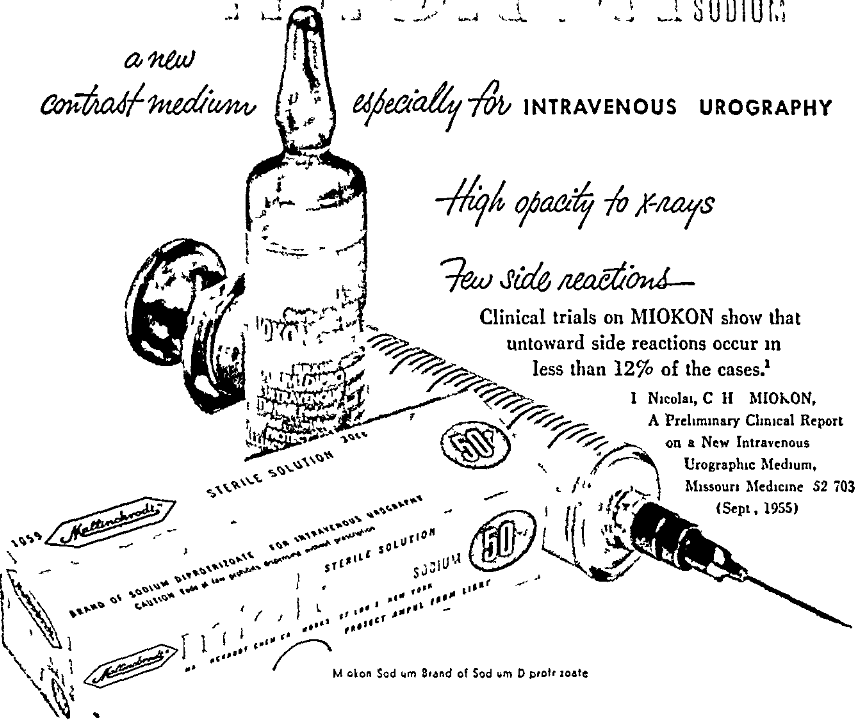

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[1] Nicolai, C H MIOKON, A Preliminary Clinical Report on a New Intravenous Urographic Medium, Missouri Medicine 52 703 (Sept, 1955)

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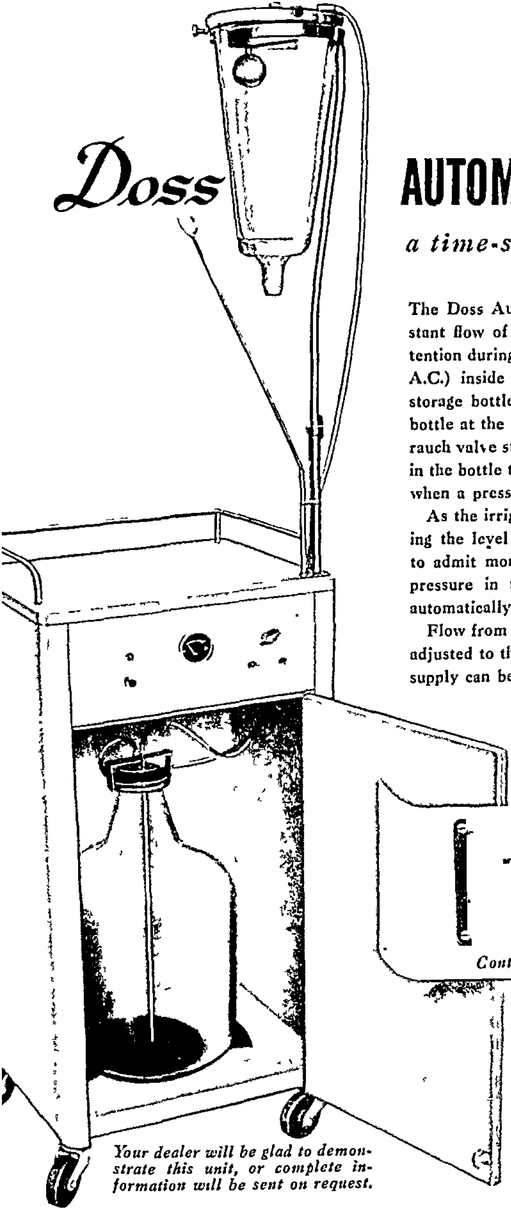

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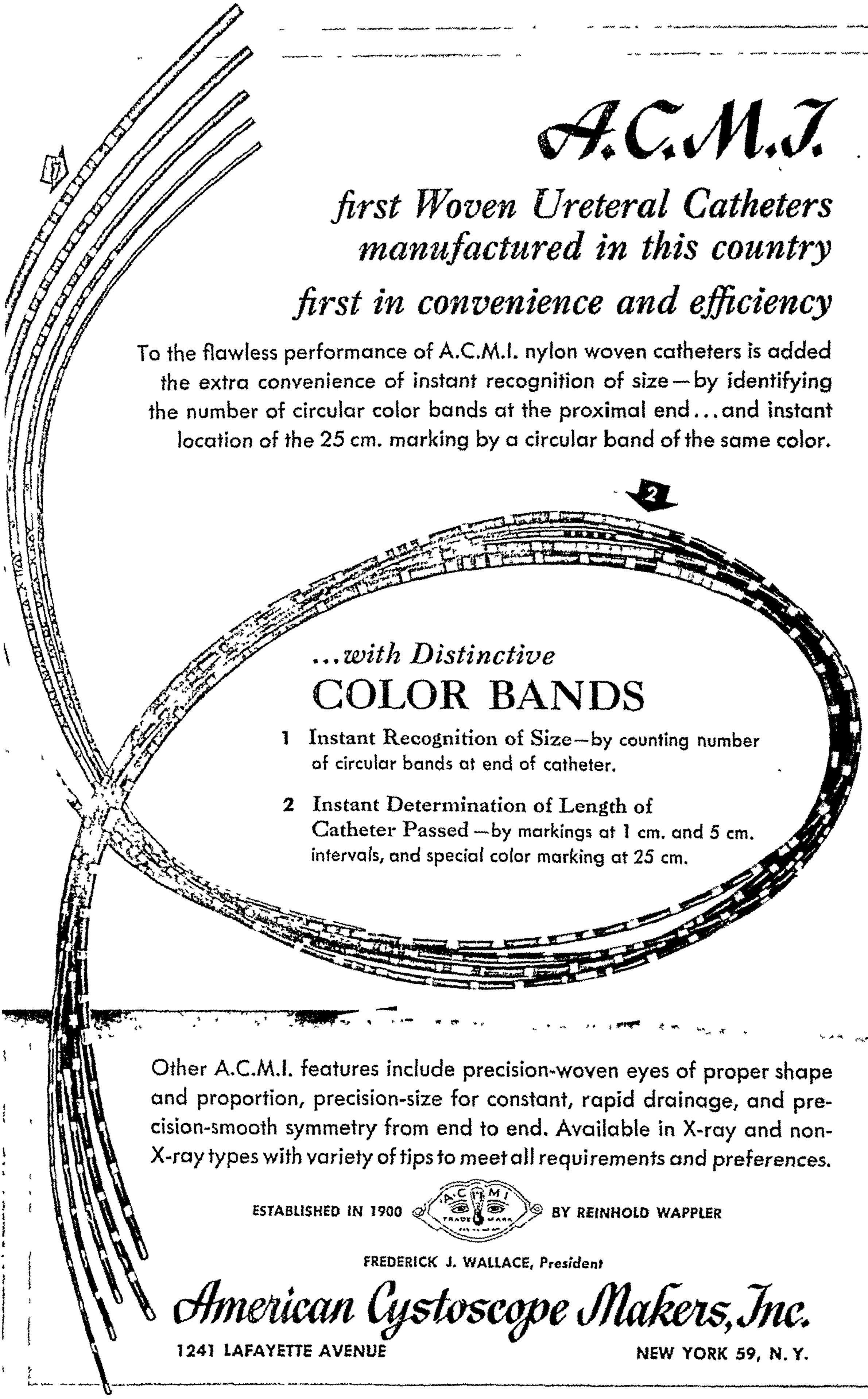

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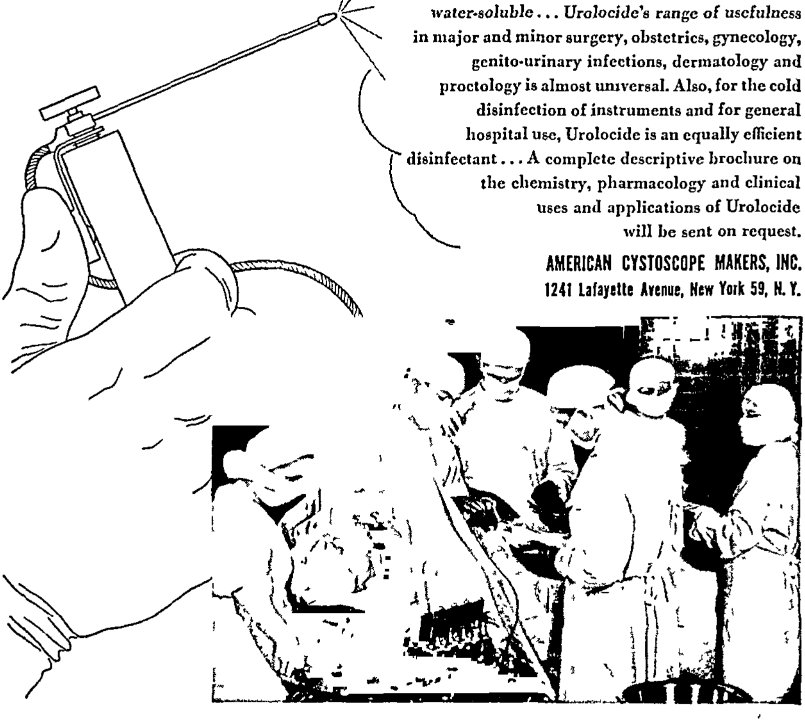

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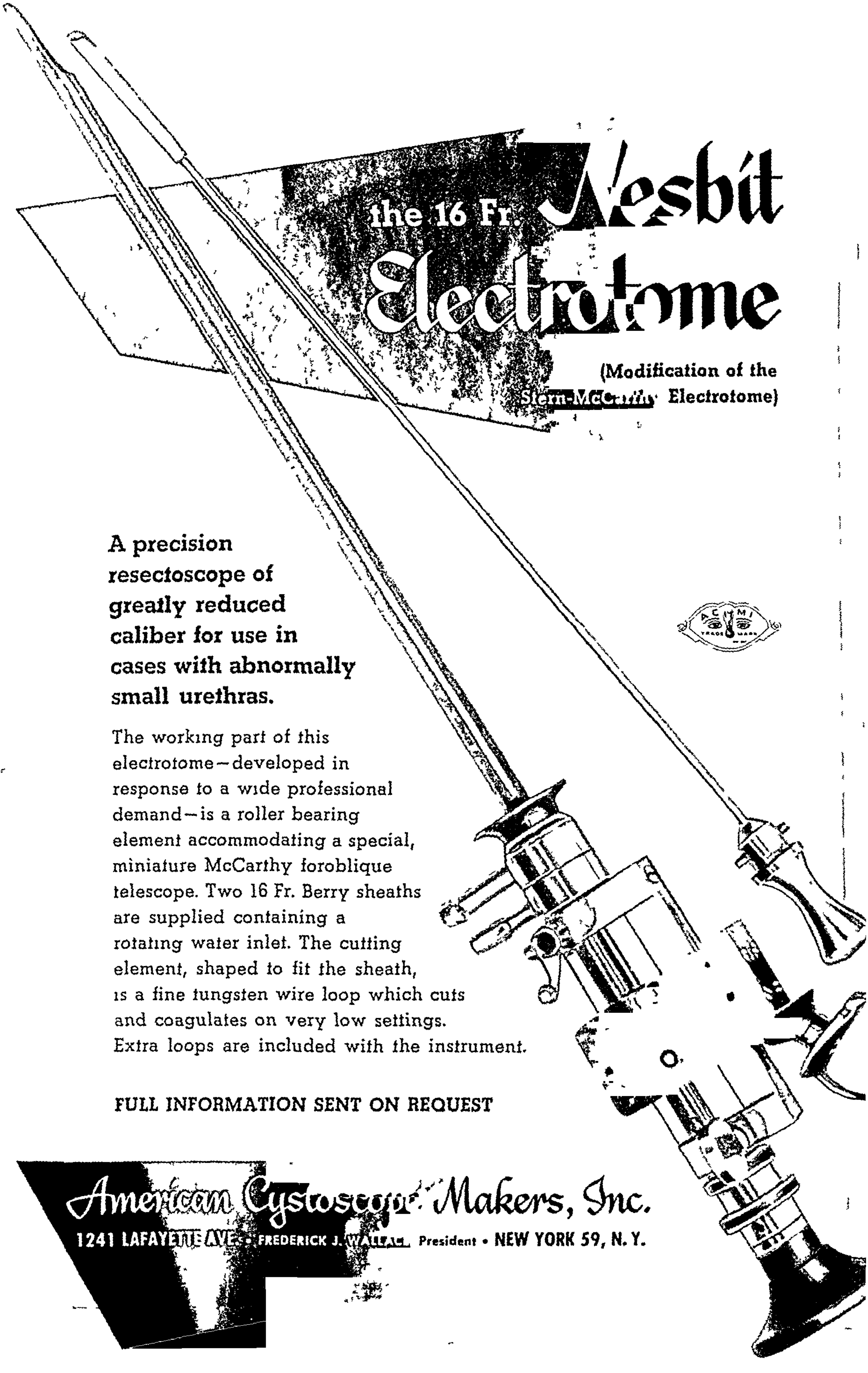

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The Journal of Urology
Vol. 75, No. 6, June 1956
Printed in U.S.A.

BASIC ASPECTS OF RADIATION THERAPY

W. S. MOOS, Ph.D.

From the Department of Radiology, College of Medicine, University of Illinois, Chicago, Ill.

The technique and use of radiation in the management of human diseases has progressed so fast in recent years that it is not only of interest to the radiologist but also became of importance to physicians and specialists in other fields of medicine.

For those of you who are not familiar with or have forgotten the fundamental concepts of radiation physics, I would like to discuss very briefly what type of radiations are available and also their characteristic properties.

One has to distinguish between two main types of radiation: electromagnetic radiation such as x-rays and gamma rays and also particle irradiation.

Electromagnetic radiation is characterized by the fact that energy is transported in form of electromagnetic waves. These waves are similar to those emitted by a radio station or by a light source. However, they differ from those by the fact that they have a much shorter wave length. Under wave length we understand the length in space of one complete wave motion, that means the distance between one "wave mountain" to the next. Radio waves can be from several hundreds of yards to a few centimeters long, the light waves visible to us are only a very small fraction of a centimeter. Since the waves become shorter and shorter as we travel down along the entire spectrum, we will pass the region of ultraviolet and come to the zone where we can speak of soft x-rays. The shorter the waves are the more penetrating, or in other words the more energetic become the x-rays. This energy – penetrating power relationship is of greatest importance in the prospect of building radiation equipment fit for various purposes.

The second means of using radiation is the application of fast moving atomic particles. Such particles are extremely small, since they are only building blocks of atoms. An atom consists of a nucleus surrounded by a number of swirling tiny matter specks carrying negative electrical charge which we call electrons (fig. 1). They have about $\frac{1}{2000}$ the weight of a positively charged hydrogen nucleus (a so called proton). The nucleus itself consists with the exception of hydrogen of several particles such as protons and neutrons. One also assumes that a neutron is composed of a proton and an electron. It has almost the same weight as a proton but is electrically neutral. Therefore electron radiation can originate either from the outer shell of an atom or from the disintegration of a neutron. The latter source of electrons is usually called beta particle radiation. A combination of 2 protons and 2 neutrons forms a helium nucleus, many of which are emitted also in the radioactive decay of radium. There they are called alpha particles. Many of these particles travel usually at very high speeds through their surroundings, having therefore a large amount of kinetic energy. Naturally, this energy is not identical for all particle sources. Here again we find a similar

Read at annual meeting of North Central Section of American Urological Association, Chicago, Ill., October 1, 1955.

Fig. 1

phenomenon as in the case with x-rays. The more energy the particles have or the faster they move the deeper they can penetrate into matter. On the other hand, the larger the particle the greater the difficulties to penetrate into any material.

In contrast to x-rays all particles have a definite range of penetration as a function of their energy. Theoretically absolute total x-ray absorption takes place only in an infinite thick absorber. Another difference between x-rays and particles except if electrically neutral is the fact that the latter can be deflected from their path by electrostatic or electromagnetic forces which have no effect on the x-rays. This is clearly demonstrated in figure 2 where the gamma rays (very energetic x-rays), alpha and beta particles emitted from a radium source pass through a magnetic field. The particles are deflected due to their different electrical charges (alpha—positive, beta—negative) in opposite directions, whereas the gamma-beam travels straight ahead.

Up till now we only spoke about radiation without considering the fact that they must be produced in some manner. Production of x-rays in machines is based on the physical law that any fast enough moving particle, e.g., electrons, converts its kinetic energy into heat and electromagnetic energy (x-rays) if it impinges on matter and is thereby stopped. The higher the atomic number of the stopping material the more x-rays are produced. The faster the particle was originally the more penetrating the x-radiation. In natural and artificial sources such as we find in radium the gamma rays are produced by the release of surplus energy in an unstable atom which tries to decay into a more stable form.

In x-ray generators one accelerates electrons through an evacuated glass tube by means of a high electric potential across the accelerating tube. The positively charged electrode in the tube is provided with a target which will be the origin of the x-rays. The positive electric potential will cause the electrons to travel faster and faster toward the target the higher the potential is made. One can achieve high potentials by several means. Standard x-ray therapy equipment uses high voltage transformers. (The energy of all x-rays can be expressed in wavelength [cm.] but it is more common and easier to use the applied accelerating potential in volts in order to define the x-ray energies.) One has succeeded in building transformer-fed equipment up to more than 400,000 volts. However, attempting to go into the million volt range one runs into trouble with breakdown of insulation, etc.

To overcome these difficulties several new means were developed. One of them is the electrostatic generator which will produce x-ray beams of several million volts. Figure 3 shows such an installation. Electrical charge of either sign, depending on whether one wishes to accelerate positive particles or negative electrons, is sprayed on an endless rubber belt. Let us assume we accelerate electrons for the production of x-rays. Negative charge travels from the corona points to the fast moving belt and is carried up to a metal dome which is highly insulated from the ground. In this manner a very high negative potential in comparison to the ground potential can be collected in the dome. This potential of several million volts allows the acceleration of electrons emitted from a heated filament inside a long evacuated glass tube since the target which is at ground or zero potential seems to be positive for the electrons relative to the

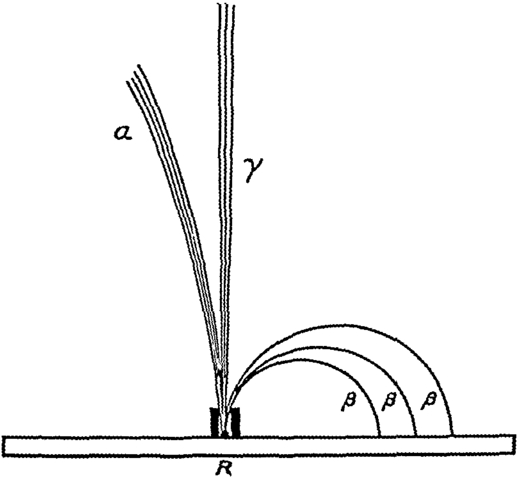
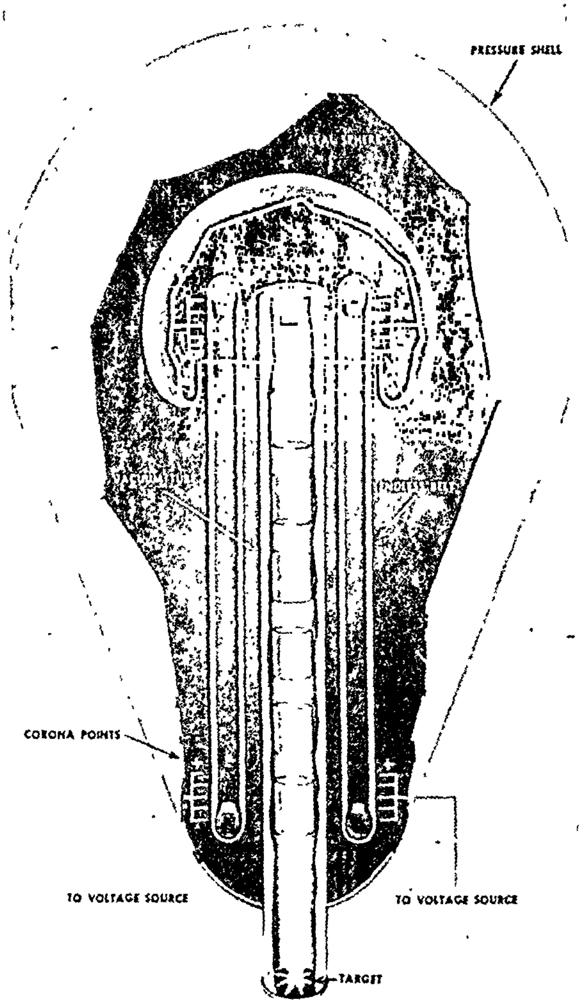


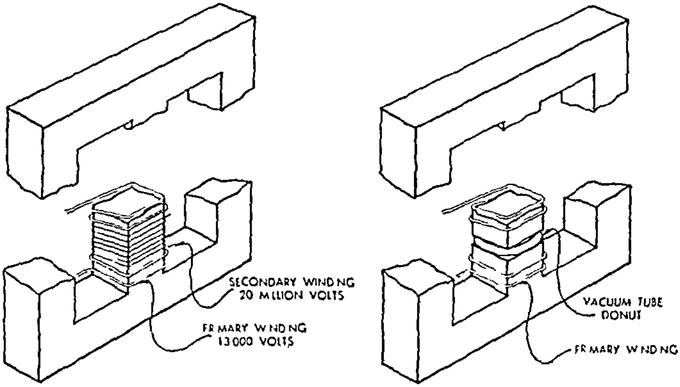
Fig. 2. Deviation of a and β particles by magnetic field perpendicular to plane of paper, γ radiations are not deviated.



THE VAN DE GRAAFF GENERATOR

FIG. 3

dome. As the fast electrons, traveling almost with the speed of light, hit the target and are stopped therein, a powerful x-ray emerges from the tube. If one removes the target the possibility of electron-beam treatment is given. Penetration depth of electrons can be roughly estimated to be about ½ cm. (water) per 1 million volts. Quite a number of such generators are now in use in hospitals but have found some competition from the cobalt 60 bomb. We know that Co 60 has similar properties like radium. It emits gamma rays of almost the same energies and can be artificially and relatively cheaply produced in large amounts in nuclear reactors. The highly radioactive source is planted inside a protective lead shield and needs practically no service of complicated machinery. The only drawback is that the amount of the useful radiation will have decreased to one half of the original intensity after about 5 years and also that no electron beam can be produced.



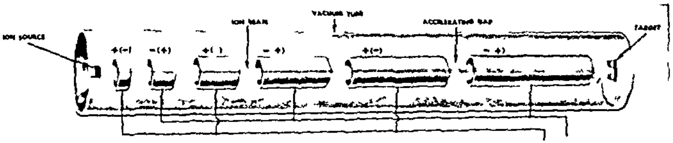
SCHEMATIC TRANSFORMER

SCHEMATIC BETATRON

Fig 4

Exceeding the energies of such sources as just discussed are those generated by the betatron and linear accelerator A betatron can be considered in a way as a converted transformer The secondary high voltage coils are replaced by an evacuated doughnut shaped porcelain tube (fig 4) The primary (low voltage) coils cause a strong fluctuating magnetic field in the laminated core which in turn forces the electrons, injected into the tube, to follow a circular path and at the same time increases their velocity every instant they complete their circle For instance if they rotate 200,000 times and gain an average of 100 volts per turn they will finally end up with an energy of 20 million volts At the instant the maximum is reached, an electronically controlled pulse will cause a momentary decrease of the magnetic guiding forces and the orbit of the racing electrons expands due to the centrifugal forces on the particles This will cause the electrons to strike an obstacle in the form of a target In this way one obtains even more powerful x rays

A linear accelerator, whose principal system is demonstrated in figure 5, can also produce x rays which are just as powerful as those from betatrons Both of them in addition allow extraction of electron beams used in experimentation and the treatment of cancer The even numbered cylindrical electrodes mounted inside the evacuated tube are wired together and so are the odd numbered



THE LINEAR ACCELERATOR

Fig 5

electrodes. Both rows of electrodes are connected to a high voltage - high frequency oscillator. In this arrangement, each set of electrodes changes its either positive or negative high potential continuously at a speed determined by the high frequency generator. An electron leaving a hot filament at the beginning of the tube would be attracted by the first electrode while the latter is positively charged. As this electrode becomes negative while the electron traverses the cylinder, the next electrode becomes positive and the electron obtains further acceleration. This process is repeated over and over again until the final desired energy of the electron is reached. Since the particles travel faster and faster through the cylinders with each accelerating stage, these electrodes must become increasingly longer in order to keep the whole procedure in rhythm. Again the electrons hit a target after final acceleration or are allowed to emerge through a thin aluminum window.

In the discussion of radiation sources we have to consider not only x-ray machines but also natural occurring radiating elements such as radium and radon, as well as artificially produced radioactive isotopes. One of the latter we mentioned briefly before in the description of the cobalt bomb. Cobalt 60 as well as radium can be used in form of needles, plaques, capsules, and other forms of applicators. However, cobalt has the great advantage of being much cheaper, easier to handle, and can be made into almost any desired form and shape.

Radon seeds have the advantage that one is able to leave them in the treated site since they decay very fast, leaving almost no radioactivity after a few weeks. However, they are relatively complicated to produce by pumping radon gas from a large radium source into the proper capillary tubing, which then has to be sealed and calibrated. Furthermore, this requires expensive installations and protective measures not to speak of the great initial investment in the radium source.

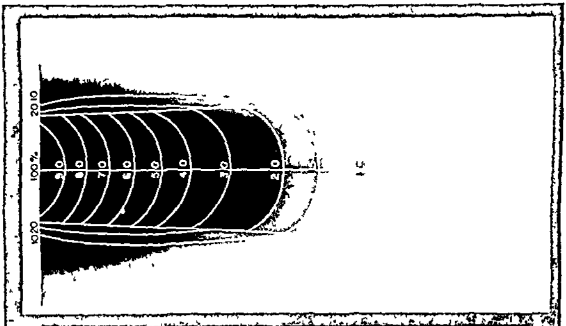
Nowadays these difficulties and costs have been considerably reduced due to the availability and use of radioisotopes such as gold 198 and yttrium 90. These isotopes have about the same characteristics as radon as far as radiation and life is concerned. But cobalt 60, gold 198 and yttrium 90 are not the only available new sources for use in medicine. Almost all isotopes of any element have some application, be it for diagnostic, therapeutic or research purposes.

Perhaps at this point I should explain what radioactive isotopes actually are. Let us consider a simple hydrogen atom. Such an atom consists of an electron spinning wildly around the nucleus which is in this case only a positively charged heavy particle, a proton. Now if one tries to change this nucleus by shooting neutrons into it, be it in an atomic reactor or some other device, the nucleus will capture eventually such a neutron and we obtain the so-called heavy hydrogen. This heavy hydrogen or also sometimes named deuterium, has still the same atomic number and therefore is chemically the same as ordinary hydrogen. However, physically it is different, because its atomic weight has become larger. Heavy hydrogen is an isotope of the common hydrogen. Such changes can be achieved by neutron bombardment in almost all elements of the periodic system. Some of these elements have only one and some quite a number of isotopes.

Heavy hydrogen is not radioactive. Why? It is a stable isotope! As long as the ratio of the number of protons to the number of neutrons is one or close to one, the isotopes do not disintegrate. However, if the binding forces which keep the nuclei together are weakened by adding an excess of neutrons, the atom decays and we have a radioactive isotope. All such active isotopes attempt to reduce their structure to a stable existence. This means that all radioactive material will after a certain time become entirely inactive. Since some radiating elements decay extremely slow and some in a few seconds, one has chosen a more convenient time scale, namely, the time which is necessary to reduce a certain amount of radiating matter to half its original activity. This one calls the half life time which is characteristic for each single radioactive isotope.

An example of a long half life is the one of radium. Radium will have lost half its activity after 1622 years. However, radon will decay to half its original value after 3 days and 18 hours.

Now since we have discussed the various sources of radiation let us go over to their actual application. Most commonly used is the standard 200,000 volt x-ray therapy unit. In figure 6 one can see the distribution of an x-ray beam produced by such equipment in tissue. It becomes immediately evident that the highest dosage of radiation lies on the surface, that means in the clinical case the skin of the patient. If the site to be treated does not lie too deep inside the body, one is able to irradiate this point without overexposing too seriously the skin at the entrance port. Erythemas, more or less severe, are however in most instances unavoidable while delivering a cancerocidal amount of radiation. The problem becomes even more difficult if the x-rays have to pass not only through soft tissue but also through bone before it reaches the tumor. Bone absorbs



DENSITY DISTRIBUTION OF 200 KV X-RAY

Note: 1. High entrance dose on left
2 Side scatter.
3 Limited penetration.

FIG. 6

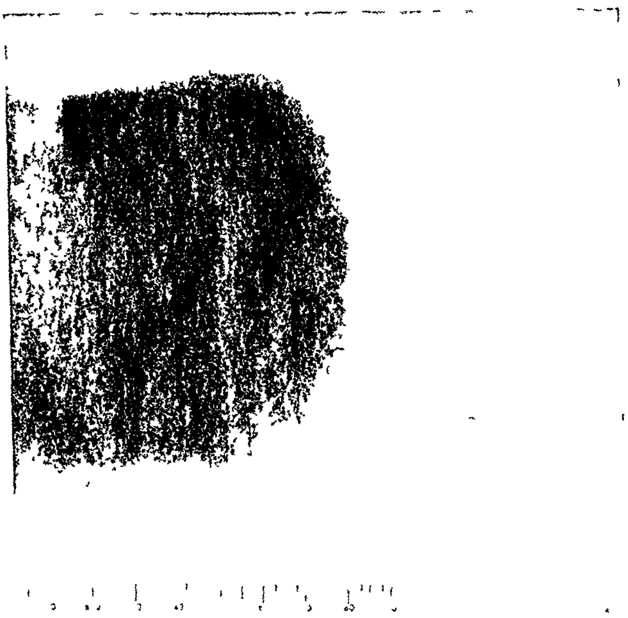


FIG 9

Since many institutions have neither the interest nor the means of acquiring high energy radiation generators, they might still have a great opportunity by the use of radioactive isotopes. I would assume that it is fair to place radium and radon into this area of interest, as they are naturally occurring radioactive substances. As said before Ra and Co 60 have almost identical properties in their use as therapeutic instruments. Only cobalt sources are cheaper, but have a half life of about 5 years, in comparison with radium's 1600 years. Radium as well as cobalt are almost entirely employed for therapeutic use. They are applied internally in most cases. The advantage of such sources is the rather localized area of treatment, since the fall off of the radiation is quite rapid around a radium or cobalt needle. This fast disappearance of radiation is not due to absorption alone but is caused by the inverse square law effect. All x-ray or gamma ray beams follow this law but its effect becomes extreme if one comes very close to the radiating source itself. It means that the intensity of the radiation decreases with the square of the distance, e.g., if one measures 100 per cent units of radiation at 1 cm. from the source one will find only 25 per cent units at a distance of 2 cm.

Next frequent to radium or cobalt 60 is the application of radon. Again this source is used in interstitial therapy. It has one great advantage over the ones previously mentioned, simply for the reason that once deposited in the form of seeds at the desired location, one can leave it there, whereas radium and cobalt must be removed to avoid overexposure. Radon has a half life of 3 days and 18 hours and that means after 25 days less than 1 per cent of the original activity is left.

However, radon has found a strong competitor in gold 198. Gold seeds activated in the atomic pile are used in the same manner as radon. In addition to

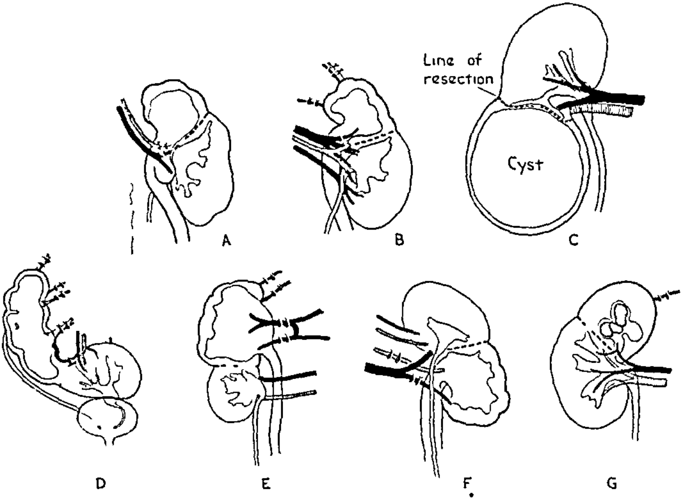


FIG 1 Renal resection Schematically indicating manner of vascular ligation to minimize renal bleeding upon bisecting kidney This calls for clean precise dissection of entire renal vascular supply so that no important nutrient vessel is accidentally divided These schemas were originally drawn immediately after operation in each case

reduplication for the opposite upper urinary tract may be anomalous or even congenitally absent, or important malformations may coexist in the lower urinary tract In the two young surgically treated patients reported here, and a third not operated upon, each was initially examined because of persistent pyuria which for weeks or months had been clinically designated as chronic "pyelitis" Urologic examination revealed that the urinary tract on one side was not only anomalous but so hopelessly injured by congenital obstruction and complicating infection as to demand total excision It was also found that half of the remaining reduplicated kidney was gravely diseased and required removal by uretero heminephrectomy Naturally one undertakes such procedures on a solitary kidney with some trepidation but it is a chance that must be taken and in general offers a vastly improved prognosis As a matter of urologic interest and to encourage others who may be confronted with a similarly discouraging urosurgical problem, the clinical data and surgical program are presented together with a satisfactory followup of over five years in one of these children and more than seven years in the other These patients, each of whom I have mentioned by illustration elsewhere,[1] lend encouragement to the urologist's increasing tendency to conservative renal surgery and are of sound teaching value because of the reasonably long period of followup observation It is recognized that patients with such limited remaining renal volume are necessarily living in constant jeopardy, particularly from the dangers of intercurrent infection, especially is

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[1] Campbell M F Clinical Pediatric Urology Philadelphia W B Saunders Co , 1951

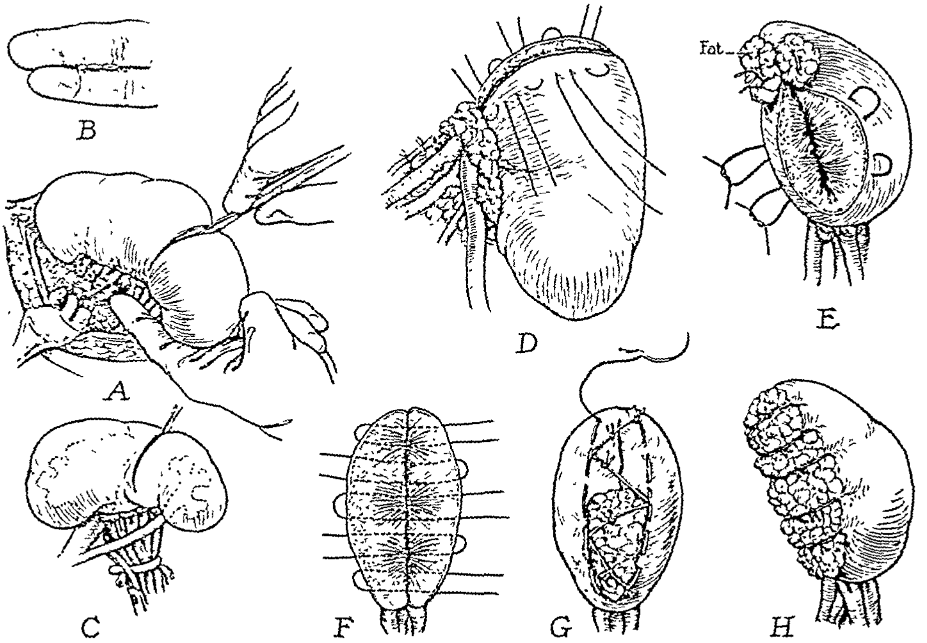

Fig. 2. Renal resection and methods of renal suture. *A*, renal resection with digital compression (*B*) of the pedicle to the segment to be preserved. *C*, pedicle compression using a soft rubber tourniquet and with extremely gentle pressure. *D*, kidney resected. Reversed mattress sutures are tied on alternate sides with a piece of fat, living muscle, sheaf of catgut, or oxidized gauze placed beneath the ligature loops to prevent their cutting through. *E*, *F*, schema of *D*. *G*, renal suture line partially closed; long ends of reversed mattress sutures are alternately tied together across wound with fat or oxidized gauze placed beneath. *H*, renal suture completed. Author has found this simple method most satisfactory in nearly sixty cases.

this so in the young who have ahead of them as potential afflictions the contagious and exanthematous diseases. This is particularly true as concerns measles and scarlet fever which are notoriously apt to cause serious renal complications—notably acute nephritis.

While it is true that some hyperplasia of the remaining renal segment takes place when the resection is carried out while the patient is very young, this favorable factor is somewhat neutralized by the increased danger of infection and toxic renal trauma consequent to the common childhood infections and disease.

CASE REPORTS

Case 1. P. D., a male aged 30 months, was referred to me on April 27, 1948 by Dr. Robert O. Y. Warren of Wilmington, Delaware for urologic examination because of persistent pyuria with recurrent attacks of severe "acute pyelitis" beginning at the age of 6 months.

When first seen by me after this admission to the hospital (April 27, 1948) the child was found to be desperately sick, extremely urotoxic, and the temperature ranged over 104F. His abdomen was tensely distended. After a 48-hour recuperative period during which fluids, penicillin, and streptomycin were administered and his bowels were well evacuated, a complete urologic examination was carried out.

The diagnostic study (April 29) disclosed congenital valves of the prostatic urethra, the unusually deep type 2 leaflets extended from the proximal verumontanum back into the vesical outlet with small, deep, type 1 leaflets extending from the anterior verumontanum forward to the lateral urethral walls The verumontanum was somewhat larger than normal but the rigid bladder neck was not dilated The bladder wall showed advanced trabeculation with innumerable cellules and saccules There was also generalized severe chronic cystitis with pronounced edema over the bladder floor which made impossible an accurate estimation of the degree of hypertrophy of the trigone

Because of the extreme trabeculation and loss of the usual normal vesical landmarks by inflammatory edema the left ureteral orifice could not be found even with chromocystoscopy On the right side there was a large ureterocele which extended well down to the vesical outlet A second right ureteral orifice behind the ureterocele mass was not recognized at this time

Since the boy was in chronic complete vesical retention except as relieved by catheterization, cystostomy drainage was instituted at once to permit removal of the indwelling catheter Digital examination through the open bladder confirmed the large size of the right ureterocele which was drawn into the bladder opening and its crown cut off to establish free drainage from its ureter and pelvis When this ureterocele was opened, there was a rapid outpouring of at least four ounces of extremely thick, foul, green pus Through the opened uretero cele a 14F two eye latex catheter was passed upwards to the infected hydronephrotic pelvis which was later proved to be the upper of reduplicated right renal pelves (fig 3, *B*) An excretory urographic study made before I saw the boy had shown a relatively normal but slightly lower and larger than usual right pelvis which proved to be that of the lower half of the kidney (fig 3, *A*) On the left the kidney showed far-advanced hydronephrosis and hydroureter apparently above a ureterovesical junction stricture, a diagnosis subsequently verified (fig 3, *C*)

On May 11 high left ureterostomy was performed, a 14F latex catheter was passed upwards to the pelvis and anchored while a second catheter was passed down the ureter towards the bladder and anchored The excessive remaining right ureterocele segments were excised

Two weeks later (May 25) the upper half of the infected, hydronephrotic, hopelessly injured right kidney was resected together with its ureter nearly down to the bladder wall (fig 3, *C*)

Histological examination of the removed right upper renal segment was made Diagnosis Chronic pyelonephritis, severe, infected hydronephrosis, severe, chronic ureteritis

After 2 months of free drainage by ureterostomy, the left kidney still showed almost no function, and only hopeless destruction by severe, long standing obstruction and infection On June 10 left ureteronephrectomy was performed, removing the greatly dilated ureter down to the bladder The histologic features of the removed left kidney and ureter were essentially the same as previously described for the resected right upper renal segment and its ureter

Following the left ureteronephrectomy, the suprapubic tube urinary drainage gation disclosed a veritable museum of urinary tract anomalies, most of which were correctable by excision, cautiously with multiple stage surgical treatment. This case demonstrates how relatively little sound renal parenchyma will support life and foster apparently good physical development. In case 1, after 7 years there is no suggestion of renal rickets or renal dwarfism; the blood calcium: phosphorus values and ratio remain normal. The blood nonprotein nitrogen is but slightly elevated above normal, and the phenolsulfonphthalein output estimation is within normal limits. The far more sensitive test of renal capacity—the urea clearance study—reveals reduced renal function as does specific gravity fixation around 1.010. The blood pressure is normal.

Case 2. B. C. a girl, aged 3 months, was referred to me on November 2, 1949 by Dr. William Shields of Providence, Rhode Island for urologic study because of persistent pyuria practically since birth and with questionable retardation of growth.

November 3, 1949: Abdominal palpation disclosed an unusual fullness in the right side but no kidney as such could be felt. Squeezing of the lower abdomen caused considerable extremely purulent urine to squirt out from an ectopic (urethral) ureter opening.

Cystoscopic study revealed a reduplicated right ureter and kidney with advanced infected hydroureter and hydronephrosis of each segment (fig. 4, *A*). The ureter from the upper half opened into the bladder behind, and was compressed by an enormous ureterocele which filled the bladder and terminated the excessively dilated (15 ×), elongated (2 ×) and tortuous ureter from the lower renal segment. The ureterocele opened ectopic in the posterior urethra.

On the left ureterorenal reduplication also existed. There was massive infected hydronephrosis and hydroureter of the lower segment, the greatly dilated duct terminating in congenital ureterovesical junction stricture (fig. 4, *B*). The ureter and pelvis of the upper segment were normal (for the anomaly) and represented the baby's entire functioning kidney tissue.

Right ureteronephrectomy was carried out at once to eradicate what seemed to be the major focal infection, the ureter being removed down to the bladder wall (fig. 4, *C*). Much to my amazement when the kidney was exposed, a rouleau of a half dozen miniature supernumerary renal buds was found in a band of fibrous tissue which passed lateral and downwards from the lower outer cortical surface (fig. 5). The histologic diagnosis was subacute pyelonephritis; ureteritis, severe; infected hydronephrosis and hydroureter; supernumerary renal buds (fig. 6, *A*).

A week later, November 11, 1949, and with the 3½-month-old baby already greatly improved, left ureteroheminephrectomy was performed, removing the diseased lower half of the kidney and its greatly dilated tortuous ureter down to the bladder wall. The "good" upper renal segment remaining measured about 4 by 3 by 2 cm. and represented the child's only renal secretory tissue. Recovery from this second decidedly major and hazardous operation was so remarkably rapid and satisfactory that 8 days later the final operation could be performed.

On November 19 transurethral ureterocelectomy was carried out. Using a

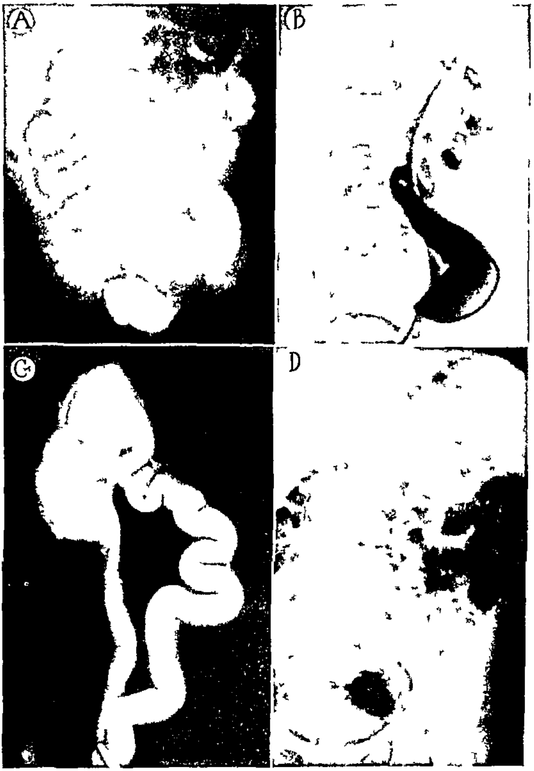

Fig 4 Case 2 *A*, coronal or "halo" outline of bladder surrounding ureterocele which filled viscus and drained upper half of reduplicated right urinary tract in a 3 month old girl examined because of persistent pyuria Entire right upper tract and lower half of left kidney were destroyed by urinary back pressure and infection, the small upper left renal segment supported life (*B*) Treatment right ureteronephrectomy (*C*, pyelogram of removed specimen), left ureteroheminephrectomy, ureterocelectomy *D*, urographic examination of remaining upper half of left kidney 6 months postoperatively

16F Nesbit resectoscope, nearly all of the right ureterocele was excised including the ectopic portion emptying into the posterior urethra There was moderate bleeding which was checked by coagulation A 16F balloon catheter was anchored indwelling for 2 days

About the time of discharge of the baby from the hospital, the reports of the histologic examination of the resected left renal tissue were received In addition to severe suppurative pyelonephritis and ureteritis (infected hydronephrosis and hydroureter, advanced), to our utter surprise an early embryonal adenomyo-

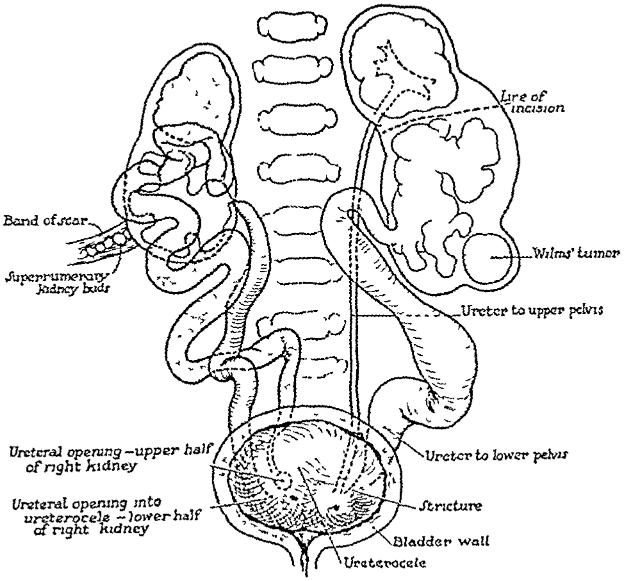
Line of incision
Band of scar
Supernumerary kidney buds
Wilms' tumor
Ureter to upper pelvis
Ureteral opening—upper half of right kidney
Ureter to lower pelvis
Ureteral opening into ureterocele—lower half of right kidney
Stricture
Bladder wall
Ureterocele

FIG. 5. Case 2. Schema of anatomic findings. Rouleau of six supernumerary renal buds was found at lower outer renal pole on right and comparably located on left (corresponding to 4 o'clock on the time piece) was an early Wilms' tumor (renal embryoma) 1 cm. in diameter. Following right ureteronephrectomy, left ureteroheminephrectomy and ureterocelectomy, only upper half of left kidney remained; 5 years later child is developing normally despite her dependence on small amount of remaining parenchyma.

sarcoma (Wilms' tumor) had been discovered in the outer lower resected parenchyma and at a point precisely corresponding contralaterally to the origin of the several supernumerary kidney buds discovered on the right side (fig. 6, *A–D*).

On January 30, 1950, two months after the last operation, the remaining portion of the left kidney was functioning well, urographically showed a normal pelvic outline for this type of kidney segment, the urine from this organ was crystal clear, but the bladder urine was slightly hazy. The electroresected ureterocele wounds had not entirely healed.

On April 1, 1954 when she had a slight flareup of infection, the urinalysis was straw color, clear, specific gravity 1.021, albumin 1+, sugar 0, white blood cells 20–30, and red blood cells 0–2 per high power field, casts none. The blood urea nitrogen was 24 mg. per cent, CO_2 combining power 28 volumes per cent, blood chlorides 103 mg. per cent, calcium 5.6 mg. per cent, phosphorus insufficient quantity for examination. The hemoglobin was 15 gm. per 100 cc of blood, and the remainder of the blood count was essentially normal. The phenolsulfonphthalein test was not completed as the child did not void sufficiently. Urine culture showed an occasional colony of nonhemolytic Staphylococcus albus and E. coli. The blood pressure was 80/50. The transient urinary infection responded readily to medication.

Three months ago, December 10, 1954, Doctor Shields examined the child 5½ years postoperatively and found that the urine culture was sterile, and reported that the girl is "a very handsome child," and that she is in excellent health with normal development for her age. She weighed 40 pounds and was attending school regularly. The blood pressure remained around 115/70 mm. Hg. The

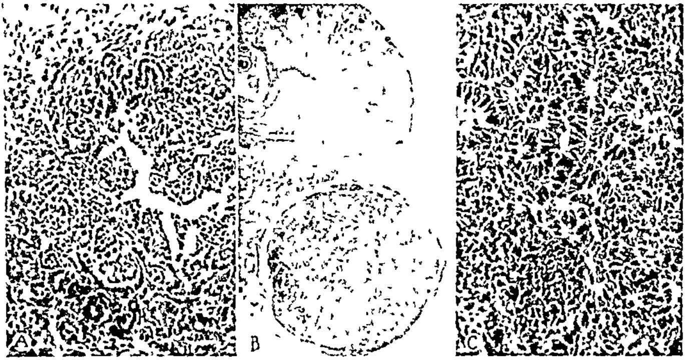

FIG. 6. [illegible] ture of one of six small supernumerary [illegible] of these accessory structures was imbed [illegible] wnward from right kidney at a point corresponding to 8 on the clock face. High magnification of center of one of these renal buds showing abortive attempts at glomerular formation about a central cavity (pelvis?) with some evidence of tubular structures. Embryonal character of tubules and glomeruli is notable. *B*, part of removed left half of kidney in which the small, round, early renal embryoma (Wilms') is shown as well as the adjacent infected hydronephrotic parenchyma. Slight tear in thick specimen is an artefact. Parenchymal renal tubules show dilation with thinning and scarring of cortex consequent to advanced hydronephrotic damage *C*, histology of the excised Wilms' tumor.

hemoglobin estimation was 13 gm. per 100 cc of blood, and there was no evidence of renal rickets. Followup excretory urographic studies have shown normal growth of the remaining renal segment with maintenance of its "normal" pelvic outlines.

On February 24, 1955 I received from Doctor Shields the following laboratory reports of recent examinations: Urinalysis: cloudy, acid; specific gravity, 1.018; albumin, glucose, casts, and microscopic examination, negative. Bacteriologic culture, E. coli isolated. Hematology: Red blood cells, 4,320,000; hemoglobin, 12 gm. (90 per cent); white blood cells, 7,200 (polymorphonuclears, 55; lymphocytes, 40; eosinophils, 1). Blood chemistry: Nonprotein nitrogen, 16.2 mg. per cent; calcium, 9.1, and phosphorus, 3.0 mg. per cent. Renal function test· Phenolsulfonphthalein output, first hour, 125 cc, 70 per cent; second hour, 55 cc, 25 per cent; total output, 95 per cent. Blood pressure, 117/70 Hg.

Comment. It is notable that in case 2 the child not only survived operation by virtue of half of one kidney but, equally encouraging, she appears to be cured of a highly malignant embryonal adenomyosarcoma or Wilms' tumor of unfavorable prognosis removed in the resected renal segment. Because of her relative paucity of renal parenchyma, however, it would be unwise for her later to become pregnant; it seems wholly unlikely that the small amount of renal tissue she has would see her through even an uncomplicated pregnancy.

Case 3. L. M., a girl aged 4½ years, was first seen by me on August 16, 1954 with a story of crying on urination for 15 months but no dysuria. During this time she had been subjected to urologic examination by several eminent urologists in the New York metropolitan area but apparently no definitive diagnosis had been established. On one examination a month before I saw her she was said to have 22 ounces of infected residual urine, and a contracted bladder outlet; dilation of the urethra had been advised.

My examination on August 17 disclosed a residuum of 19½ ounces of pea-souplike urine, culture of which showed a nonhemolytic Staphylococcus aureus infection and later E. coli. The blood nonprotein nitrogen was 45 mg. per cent, the CO_2 combining power 42.8 volumes per cent, and the blood count revealed mild anemia.

The study also revealed a congenital contracture of the bladder outlet. The vesical interior was entirely anomalous with a subvesical and subtrigonal diverticulum 4 cm. in diameter. Additional diagnoses included chronic urinary infection, right ureterovesical junction stricture with massive hydroureter and hydronephrotic destruction above (pyuria 4+; fig. 7). There was left ureteropelvic reduplication with ureterovesical junction stricture of the greatly dilated tortuous ureter of the lower infected renal segment which showed far-advanced hydronephrosis (pyuria 4+; fig. 7). The urine from the other left ureter (superior renal segment) was clear and sparkling, and the pyelographic demonstration was normal for a reduplicated upper renal segment. Intravenous indigo carmine showed only the faintest return from the right kidney and lower half of the left, but the dye return from the left renal upper half was deep and in normal appearance time.

The treatment advised included initial cystostomy drainage with subsequent

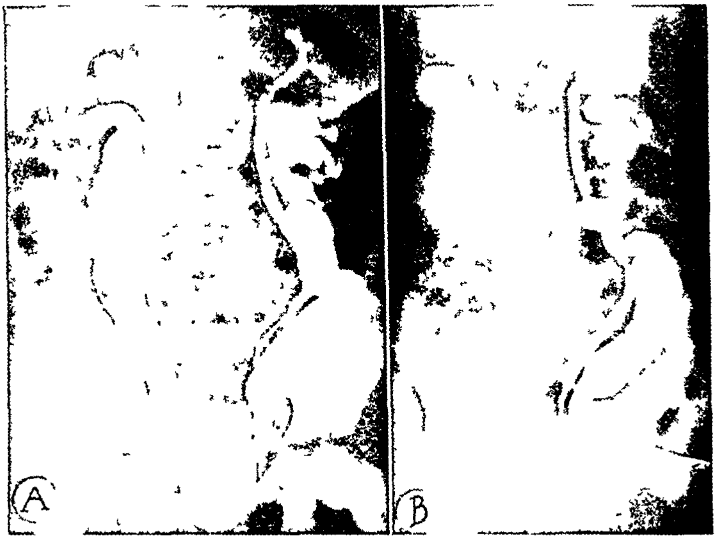

Fig. 7 Case 3 Urographic demonstration in a 4½-year-old girl examined because of persistent pyuria and crying on urination. Anatomic diagnosis Congenital stricture of bladder outlet with 19½ ounces residual purulent urine; subvesical diverticulum, right ureterovesical junction stricture with massive hydroureter and hydronephrotic destruction above, left ureteropelvic reduplication with ureterovesical junction stricture of greatly dilated tortuous ureter of lower infected hydronephrotic renal segment and, finally, small upper renal segment, urine from which was clear and sparkling and function of which supports patient's life *A*, anterior-posterior exposure; *B*, oblique view.

transvesical resection of the vesical outlet (contracture), transvesical diverticulectomy, right ureteronephrectomy, left ureteroheminephrectomy, and chemotherapy

The diagnosis having been established and the surgical treatment advised, the parents took the child home to another part of the country, I have not been able to obtain further data in this case

SUMMARY

The anatomic and surgical complexity of the 3 cases reported here exemplify the large number of congenital urinary tract lesions commonly manifested by persistent pyuria which, in turn, is generally inadequately designated and treated as chronic "pyelitis" Such examples further emphasize the responsibility of the general practitioner, pediatrician and/or urologist to insist that complete urologic investigation be carried out in all children with persistent pyuria not cured in two to three weeks with intensive present-day chemotherapy or antibiotic therapy Here, at least one and preferably two negative cultures of aseptically collected urine should be the test of cure

In chronic pyuria in the young, medical therapy having failed and the anatomic diagnosis having been established, the urologic treatment may be as simple as urethral or ureteral dilation together with further intensive chemotherapy On the other hand, as in the cases here reported, it may be necessary to carry out major procedures as bladder neck resection, diverticulectomy, ureterostomy, nephrectomy, ureteronephrectomy, heminphrectomy or, of lesser hazard, transurethral resection of prostatic urethral valves In most of these infants and children such treatment when necessary may be expected to convert an utterly hopeless prognosis to a favorable one

Alfred I duPont Bldg , Miami, Florida

THE JOURNAL OF UROLOGY
Vol. 75, No. 6, June 1956
Printed in U.S.A.

SIMPLE RENAL CYSTS IN CHILDREN: REVIEW OF THE LITERATURE AND REPORT OF FIVE CASES

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Small, congenital, simple renal cysts are not unusual in children (2 to 4 per cent on the basis of postmortem evidence [Campbell]) but they rarely attain sufficient size to become clinically evident in childhood, as demonstrated by the paucity of reports of such cases in the literature. We were able to find only 16 recorded cases of simple renal cyst in children through the age of 14 years. Data on these cases plus 5 cases we wish to add are summarized in table 1.

Of 153 cases of solitary renal cyst on which data were collected by Carson in 1928, only four were in children. Braasch and Hendrick, in 1944, found that only four of 163 solitary cysts occurred in patients less than 21 years of age. This bears out the statement that it is essentially a "disease of adult life (Kretschmer)."

Various classifications of renal cystic disease have been proposed. Braasch and Hendrick classified the lesions as follows: 1) retention or inflammatory cysts, 2) simple cysts, 3) peripelvic cysts, 4) parapelvic cysts, 5) cysts secondary to pathologic changes in the kidneys and 6) polycystic lesions. They subdivided the simple cysts into single, multiple, multilocular and hemorrhagic. Campbell distinguished the following congenital groups: 1) congenital solitary renal cysts, 2) multilocular cysts and 3) polycystic disease. Most writers agree that multilocular cysts are a distinct entity (Meland and Braasch; Frazier). Some consider them a variation of simple cysts (Campbell; McCrea; Lynch and Thompson), and others relate them more closely to polycystic disease (Frazier).

Although the term "solitary cyst" is frequently used synonymously with the term "simple cyst," it is not preferable, for frequently the lesion is not single. The disorder consists of a large serous cyst located in any portion of the kidney and occasionally accompanied by other, smaller, serous cysts (Herbut).

The present report will be confined to a discussion of congenital simple (serous) cysts of the kidney occurring in childhood. All acceptable cases satisfied the following criteria: 1) the cyst was unilocular, 2) there was no communication between the cavity of the cyst and the renal pelvis, 3) the cavity of the cyst was lined with epithelium, 4) no renal elements were contained within the cyst, 5) a localized region of the kidney was involved, 6) the uninvolved renal tissue was relatively normal grossly or microscopically, or both, and 7) the renal pelvis and ureter were patent. Some cases included in previous studies have been excluded from this study on the basis of these criteria (table 2).

PATHOGENESIS

It is logical to assume that congenital simple cysts are explainable on the same etiologic basis as are the cysts in polycystic disease. Various theories have been

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Read at annual meeting of North Central Section of American Urological Association, Chicago, Ill., September 29 to October 1, 1955.

proposed, excellently summarized by Rall and Odel under the categories of metabolic, inflammatory, neoplastic and developmental defects At the present time the theories based upon developmental defects are most widely accepted and warrant further discussion

Hildebrandt, in 1891, suggested the widely accepted theory that cyst formation was due to failure of union between the metanephroblastemic elements (glomeruli) and the collecting tubules originating from the metanephric (wolffian) duct Obstruction of the outflow of glomerular secretion because of faulty or absent union resulted in cystic formation

Kampmeier, in 1923, suggested that "every human individual during his fetal life normally passes through a period characterized by the presence of numerous cystic renal tubules" If such tubules do not degenerate at the proper time, but continue to grow and expand, cystic changes result He later, with McKenna, reconstructed serial sections of fetal kidneys and of a polycystic kidney and concluded that the basic defect was failure of the second to fourth generations of uriniferous tubules either to atrophy or to unite with later generations of collecting tubules

In 1941, Norris and Herman concluded, also on the basis of serial-section reconstructions, that "up to a certain period in fetal life development of the kidneys was normal Degeneration and cystic changes resulted in dissociation of the nephrons into segments The continued proliferation of these segments and the retention of secretory products caused the cyst-like dilatation of the tubules and the enlargement of the kidneys"

CLINICAL FINDINGS

In the series of 21 patients included in our study the sex was specified in 18, and of these, 12 were males (table 1) The left kidney was involved in 12 of 19 cases in which the side of involvement was specified, the upper and lower poles being involved with approximately equal frequency The capacity of the cysts varied from 1 ounce to 5 pints The presenting complaint in all but two cases was that of abdominal mass Occasionally, pain also was present, usually because of preceding trauma or infection In only two instances (cases 9 and 20) was the cyst not palpable clinically In case 20 the patient had no complaints referable to the presence of the renal cyst The cyst had been discovered by her local physician by means of excretory urography done during the course of an investigation of pain located in the opposite side of the abdomen It was relatively small in size, was located at the upper pole of the left kidney and would undoubtedly have become more evident clinically in time Of interest, both nonpalpable tumors occurred in older children

Roentgenography permits visualization of either the cyst itself, as a soft-tissue shadow, or the effect of the cyst upon the configuration of the calyces and renal pelvis In many instances, damage to the renal parenchyma renders the kidney nonfunctioning as observed on excretory urography, in which case retrograde pyelography is essential to demonstrate the lesion The typical picture is that of flaring and crescentic deformity of the calyces and renal pelvis in that part of the

TABLE 1. *Reported cases, previous and present, of congenital simple cyst of the kidney in children*

Case	Author and Year	Sex	Age, Years	Site*	Size	Procedure (Result)†
1	Hawkins, 1834	M	6	RLP	5 pints	Necropsy
2	Rochet, 1910	—	1	—	"Mandarin orange"	Cyst incised (R)
3	D'Antona, 1911	—	1	—	"Large"	Cyst resected (R)
4	Weill and associates, 1912	—	8	LUP	"Adult head"	Laparotomy, necropsy (OD)
5	Mixter, 1922	F	13 mo	RLP	"Small grapefruit"	Nephrectomy (R)
6	Vonachen and Sprenger, 1927	M	2	LUP	2,000 cc	Nephrectomy (R)
7	Higgins, 1931	M	3	LLP	13 x 10 x 9 cm.	Nephrectomy (R)
8	Allen and Ragsdale, 1935	F	10	RM	30 cc	Nephrectomy (R)
9	LeComte and Whitmore, 1935	M	13	RM	4 x 3 x 4 cm.	Nephrectomy (R)
10	Chalkley and Sutton, 1943	F	11	RLP	12 cm.	Nephrectomy (R)
11	Fister, 1943	M	6	RLP	—	Surgery refused (LW)
12	Righini, 1950	M	6	LUP	"Very large"	Cyst resected (R)
13	Campbell, 1951	M	7	LUP	500 cc	Cyst resected (R)
14	Campbell, 1951	M	5 hr.	RUP	¼ of renal mass	Necropsy
15	Campbell, 1951	M	18 mo	LUP	8 cm.	Nephrectomy
16	Christeson, 1954	F	1 mo	Left	12 cm.	Nephrectomy (R)
17	DeWeerd and Simon, 1955	M	15 mo.	Left	"Large"	Nephrectomy (R)
18	DeWeerd and Simon, 1955	F	8 mo.	Left	7.5 cm.	Nephrectomy (R)
19	DeWeerd and Simon, 1955	M	22 mo.	LM	10 cm.	Nephrectomy (R)
20	DeWeerd and Simon, 1955	F	10	LUP	5 x 6 cm.	Cyst evacuated (R)
21	DeWeerd and Simon, 1955	M	7	LM	1,800 cc; 20 cm.	Cyst wall excised (R)

* RUP, right upper pole of kidney; RLP, right lower pole; LUP, left upper pole; LLP, left lower pole; RM, right midpart; LM, left midpart.

† Result in parentheses: R, recovery; OD, operative death; LW, living and well.

kidney that has been compressed by the mass. Displacement of the kidney by the cystic mass may affect its position and axis considerably as well as alter the course of the ureter, so that in the lateral projection the kidney may be found either anterior or posterior in respect to the cyst. Roentgenologic differentiation from renal neoplasm is frequently impossible, and the rarity of simple cysts in children would certainly not warrant the use of aortography for the purpose of making this distinction.

The preoperative diagnosis was stated in 16 cases, and malignancy was suspected in nine of these. In only one instance was the correct diagnosis made

TABLE 2 *Previously cited cases excluded from present study*

Author and Year	Reason for Exclusion
Wagner, 1884	Hydronephrotic upper segment (duplication) rather than serous cyst*
Albarran and Imbert, 1905	Cysts multiple author believed a variety of polycystic kidney*
Bencke, 1911	Cyst multilocular*
Bockenheimer, 1911	Probably hydronephrotic sac rather than serous cyst
Zaccarini, 1915	Cysts medullary, one in each kidney, multilocular*
Bugbee and Wollstein, 1924	Insufficient data opposite kidney polycystic or severely nephritic
Toulson and Wagner, 1942	Cyst multilocular

* Chalkley and Sutton J Urol 50 414–419 1943

(Fister), as mentioned previously. The common misdiagnosis in favor of malignancy is easily understood when one considers the rarity of congenital simple cyst in children as compared to malignant tumor (renal embryoma), which closely simulates simple cyst clinically and roentgenographically.

TREATMENT

In this series, 18 patients underwent surgical treatment, which consisted of nephrectomy in 11 cases, excision of the cyst wall in 4 cases, and incision and drainage of the cyst in 2 cases. Nephrectomy was chosen in seven instances because it was felt that the remaining functioning renal parenchyma was insufficient to warrant conservation. In 1 case nephrectomy was indicated because infection was present, while in 3 cases the reason for performing nephrectomy was not stated. The treatment of choice, provided sufficient functioning renal parenchyma is present, is excision of the presenting cyst wall as was done in 4 cases. The fact that a conservative procedure was elected in only six instances bears mute testimony to the fact that simple renal cyst occurring in childhood usually destroys much of the otherwise uninvolved renal parenchyma before it becomes clinically evident and can be properly treated, thus frequently necessitating nephrectomy for an otherwise entirely benign condition.

REPORT OF CASES

Congenital simple renal cyst in children has been diagnosed clinically and treated in 5 cases at the Mayo Clinic since 1915. Reports of these follow, the case numbers corresponding to those given in table 1.

Case 17 A 15 month old boy was first seen at the clinic on August 9, 1918, because of an "abdominal tumor," first noted 5 months previously. This mass had grown progressively during the intervening period. The child was otherwise asymptomatic.

On physical examination a large, firm, regular, somewhat cystic mass was felt in the left upper quadrant. Routine urinalysis and determination of hemoglobin gave essentially negative results. The roentgenographic appearance of the chest was within normal limits except for some elevation of the left hemidiaphragm. A clinical diagnosis of probable "benign kidney tumor" was made and exploration was advised.

On August 17, 1918, the left kidney was exposed and a large cystic tumor was found to have almost completely replaced the kidney. The tumor entirely filled the left side of the abdomen and extended beyond the midline. The renal pelvis and ureter were duplicated. Since very little renal parenchyma remained, nephrectomy was performed.

The postoperative course was uneventful and the child was dismissed on the thirteenth postoperative day. A followup letter received 14 years later disclosed that he was living and well.

Case 18. An 8-month-old girl was first seen at the clinic on February 12, 1925, because of an abdominal "tumor" on the left side. This tumor had been felt at birth by her local physician, who had thought that it represented spleen. However, 5 weeks before her admission to the clinic he had examined the child again and had referred her for treatment. The baby had been growing normally, had never experienced gross hematuria and was asymptomatic.

On physical examination a movable mass, the size of an orange, was felt in the region of the left kidney. Routine urinalysis and determinations of blood urea and hemoglobin gave essentially negative results. The roentgenographic appearance of the chest and of the region of the kidney, ureter and bladder was normal except for evidence of a soft-tissue mass in the region of the left kidney. A tentative diagnosis of renal malignancy was made and surgical intervention was advised.

On February 27, 1925, the left kidney was explored. A "cystic tumor" the size of a large orange was found and, after the fluid had been aspirated from the cyst by means of a trocar, the kidney was removed. The cyst measured 7.5 cm. in diameter and had been filled with clear fluid. The remaining renal substance had been largely destroyed (approximately 90 per cent).

The postoperative course was uneventful and the child was dismissed on the eleventh postoperative day. No further followup data were obtained.

Case 19. A 22-month-old boy was first seen at the clinic on December 30, 1942, because of a left abdominal mass that had first been noted when he was 3 months of age. His local physician had originally believed the mass to be splenic.

On physical examination a cystic mass was felt in the left upper quadrant. Routine urinalysis revealed pyuria, grade 1 (on a basis of 1 to 4). Determination of hemoglobin and blood urea gave normal results. The roentgenographic appearance of the chest was normal. An excretory urogram demonstrated a normal right kidney and a nonfunctioning left kidney, with a rounded soft-tissue mass located in the renal region (fig. 1). A tentative diagnosis of left hydronephrosis was made and exploration was advised.

On January 14, 1943, the left flank was explored surgically. A large renal cyst was found arising from a small left kidney. The kidney and cyst were excised, the latter measuring 10 cm. in diameter. The ureter was dilated, and exploration revealed intussusception of its distal end and secondary hydroureter. The ureter was divided flush with the bladder and the distal segment was ligated.

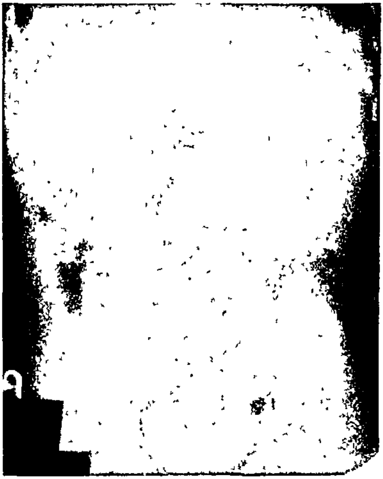

FIG. 1. Excretory urogram demonstrates normal-appearing right kidney. Large, round, soft-tissue mass occupies position of left kidney.

The patient had an uneventful postoperative course and was dismissed on the sixteenth postoperative day. No followup information was obtained.

Case 20. A 10-year-old girl was first seen at the clinic on August 21, 1951, complaining of pain in the right upper quadrant; she had had the pain for 8 months. The pain had been dull and intermittent during this period but had become more severe 2 weeks previously, during an attack of acute tonsillitis. Her local physician obtained an excretory urogram and informed the mother that the child had a "tumor or growth" in her left kidney, apparently asymptomatic, all previous symptoms having been referred to the opposite side.

On physical examination at the clinic no mass could be felt in either flank. The results of routine urinalysis, the values for hemoglobin and blood urea, the sedimentation rate, and the x-ray appearance of the chest were within normal limits. An excretory urogram revealed a normal right kidney, but there was flaring of the upper calyx of the left kidney suggestive of a tumor of the upper pole of that kidney. Cystoscopy and retrograde pyelography were performed, the latter again demonstrating a normal right kidney and a crescentic deformity of the upper calyx of the left kidney (fig. 2). A diagnosis of left renal cyst or neoplasm was made and exploration was advised.

On August 27, 1951, the left kidney was exposed and a solitary cyst of the upper pole and mesial aspect of the kidney was found. The cyst measured approximately 5 by 6 cm. Straw-colored fluid was aspirated from the cavity of the cyst, and the wall of the cyst was incised widely. Cytologic study of the aspirated fluid did not reveal malignant cells.

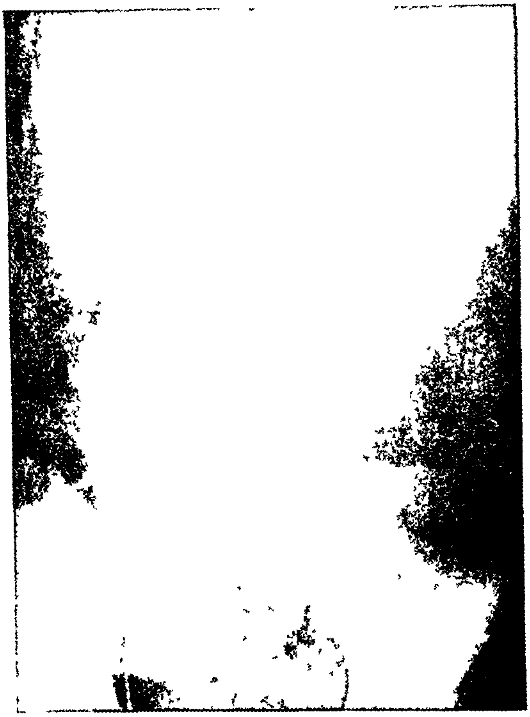

FIG. 2. Retrograde pyelogram demonstrates normal right kidney and ureter. Marked crescentic deformity involving two of upper calyceal group of left kidney is caused by poorly defined soft-tissue mass in upper pole.

The postoperative course was uneventful and the patient was dismissed on the eleventh postoperative day.

Case 21. A 7-year-old boy was first seen at the clinic on February 9, 1955, because of an asymptomatic left abdominal mass discovered by his local physician during the course of a routine physical examination. X-ray studies done at that time showed a "tumor in front of or associated with the left kidney."

On physical examination the abdomen was noted to be asymmetrically prominent, predominantly on the left side. A large mass, which was somewhat soft and nontender, occupied the entire left upper quadrant and accounted for the previously noted abdominal prominence. The results of routine urinalysis, the concentration of blood urea and hemoglobin and the x-ray appearance of the chest were within normal limits. Excretory urography demonstrated a poorly defined but definitely enlarged left renal mass, which was low-lying and which filled the entire flank. The left renal pelvis was dilated, as were the infundibula and the calyces. With the exception of the middle calyx, which was elongated and distorted, the aforementioned structures maintained nearly normal contours. The ureter was not outlined. The right kidney and ureter were normal (fig. 3, *a*). It was thought that in spite of the soft, cystic nature of the mass, the probable diagnosis was left renal neoplasm (Wilms' tumor), and surgical exploration was advised

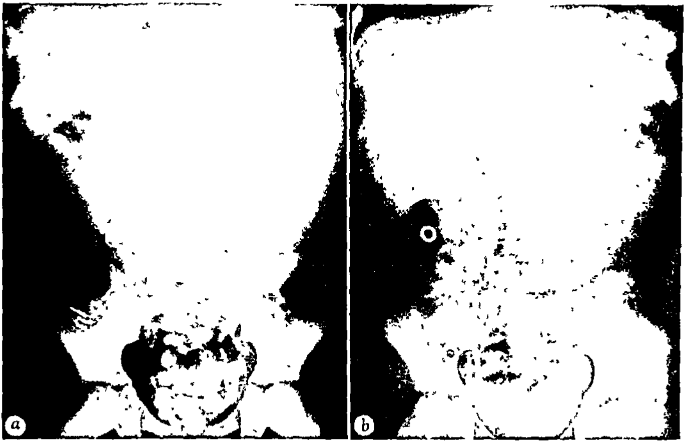

FIG. 3. *a*, Excretory urogram demonstrates grossly normal right kidney. Marked pyelectasis of left kidney along with dilatation of infundibula and calyces. Middle calyx is elongated and distorted. Enlarged but poorly defined renal mass obliterates psoas shadow. *b*, Postoperative excretory urogram shows marked improvement in appearance of left collecting system.

On February 15, 1955, exploration through a primary, left midrectus incision revealed a huge cystic mass that presented retroperitoneally and displaced the abdominal viscera to the right. The left lateral leaf of peritoneum was incised and a huge cyst, which was estimated to be 20 cm. in diameter and which arose from the left kidney, was mobilized without incident. The cyst was too large to be delivered through the incision. Renal tissue could be palpated behind this cyst, but since the status of the kidney was unknown, it was felt wise to drain the cyst. Eighteen hundred cubic centimeters of slightly yellow, clear fluid was aspirated through a trocar. After collapse of the wall of the cyst the kidney was examined carefully, and since there appeared to be nothing more than gross distortion of an otherwise normal amount of renal mass, the presenting wall of the cyst was excised. It could then be determined that this huge simple cyst had developed on the anterolateral surface of the kidney, flattening it like a pancake. The posterior surface of the kidney was normal except for its increased surface area. One other tiny cortical cyst was detected at the upper pole, and its roof was incised. The small extrarenal pelvis and ureter were normal. No communication between the cyst and the collecting system could be demonstrated. Extraperitoneal drainage was established through the left flank, following which the lateral leaf of peritoneum was closed and the abdominal incision was sutured in layers.

The postoperative course was uneventful. An excretory urogram made on the thirteenth postoperative day demonstrated an essentially normal left kidney (fig. 3, *b*). The patient was dismissed on the sixteenth postoperative day.

SUMMARY AND CONCLUSIONS

Congenital simple renal cysts that attain sufficient size to become clinically evident in childhood are rare. Sixteen cases satisfying the outlined criteria have been described in the literature and five additional cases are reported herein.

Simple renal cyst is found somewhat more frequently in males and in the left kidney. It may be encountered at any age from the newborn period through adulthood, and it involves the poles of the kidney with approximately equal frequency. The presenting complaint in almost all cases is that of abdominal mass, occasionally accompanied by pain. The lesion is demonstrable by urography, either excretory or retrograde, but roentgenographic or clinical differentiation from renal malignant tumor (Wilms' tumor) is practically impossible. For this reason, and because simple renal cyst in childern is rare as compared to renal embryoma (Wilms' tumor), the usual preoperative clinical impression is that of malignant disease.

Excision of the presenting cyst wall is the treatment of choice unless severe destruction of renal parenchyma necessitates nephrectomy. Unfortunately, such destruction frequently prevails.

The rarity of congenital simple renal cyst in children and the similarity of the resultant clinical picture to that of renal neoplasm are emphasized.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 6, June 1956
Printed in U.S.A.

DIFFERENTIAL DIAGNOSIS BETWEEN CANCER AND SOLITARY SEROUS CYST OF THE KIDNEY

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The decision whether or not to operate for exploration of a symptomless renal mass is sometimes difficult. Many of these are found incidentally in x-rays of stomach, gallbladder or spine (Ettinger and Elkin). They usually prove to be solitary, serous cysts. Operation for diagnostic purposes alone creates a low but definite rate of operative deaths and complications. If, though, there is no way to make an accurate diagnosis without operation there is much more serious danger in the possibility that a malignant lesion may be left.

We have studied the problem in two ways. First, we have analyzed the x-rays and clinical histories of 83 patients with proved diagnoses of renal cyst or cancer to see if we could find any really satisfactory criteria for differential diagnosis. Second, we have considered why, other than for diagnosis, operative exploration and excision may be justified when a renal mass is thought to be a cyst rather than a tumor.

STATISTICAL SURVEY

In 36 patients, the diagnoses of various types of renal tubular carcinoma were proved at operation. Thirty-four were subjected to nephrectomy and 2 to exploration and biopsy. Thirty-nine patients underwent surgical excision of solitary serous cysts. In 8 additional patients, the diagnosis of cyst was proved by translumbar needle puncture. The technique was that suggested by Ainsworth and Vest (fig. 1). Before injection of contrast medium a small quantity of fluid was aspirated in each case for bacteriologic, cytologic, and chemical study.

Table 1 indicates that neither the age of the patient nor the size of the mass, as outlined in x-rays, was an important diagnostic consideration.

Neither sex of the patients (fig. 2), the laterality of the lesion (fig. 3, *A*), nor the location of the renal mass (fig. 3, *B*) proved to be significant signs in differentiating the two types of disease.

In a study of clinical findings (fig. 4) we discovered several signs of presumptive but none of absolute diagnostic significance. Most of the cysts were asymptomatic. Most of the cancers caused one or more of the usual symptoms. Many more of the cancers, presumably because of their relative hardness, were discovered during routine, preoperative physical examination. The finding of anemia (less than 11 gm. of hemoglobin per 100 cc) made for strong suspicion of cancer. Eight of the cancer patients exhibited fever and in 2 it was the chief complaint.

The study was aided, in part, by a grant from the Charlton Research Fund, Tufts University School of Medicine.

Read at meeting of New England Section of American Urological Association, November 10, 1955.

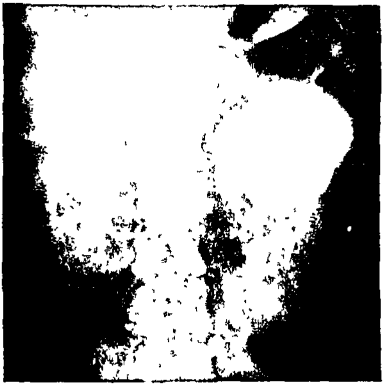


FIG. 1. X-ray of solitary, serous cyst of left kidney after percutaneous needle puncture and instillation of contrast medium.

TABLE 1

	Tumors	Cysts
Age		
Average	56	56
Range	32–84	43–75
Maximum diameter of lesion, cm.		
Smallest lesion	3	2
Largest lesion	20	16
Average	10	7

We found that retrograde pyelography offered no special advantage over excretory urography provided the latter examination was of satisfactory quality. In 7 cases of cancer, there was non-excretion of dye on the affected side and retrograde study proved mandatory. In a number of other cases we found that the retrograde study yielded sharper pictures. In 2 cases of cyst, in which both intravenous and retrograde examinations were performed, we noted distensibility of the deformed calyces (fig. 5). This has been described previously by other writers as a sign peculiar to solitary cyst. Because of the comparative rarity of its occurrence we regard the sign as having limited value.

Tabulation of extrarenal roentgen abnormalities, as seen in the pyelograms (table 2), suggested that ureteral displacement and renal axis deviation occurred about equally often in each condition. Though significant of renal mass, these signs aided little in differentiation. Changes in the psoas shadow, when found, were always associated with cancer in our group of cases.

A classification of intrarenal pyelographic abnormalities (fig. 6) shows that calcification within the mass (fig. 7) was relatively common in cancer but did not occur, in this group of patients, among those with cysts. It is of known rare occurrence in solitary cysts (Kirwin). Most of the masses whose shadows were

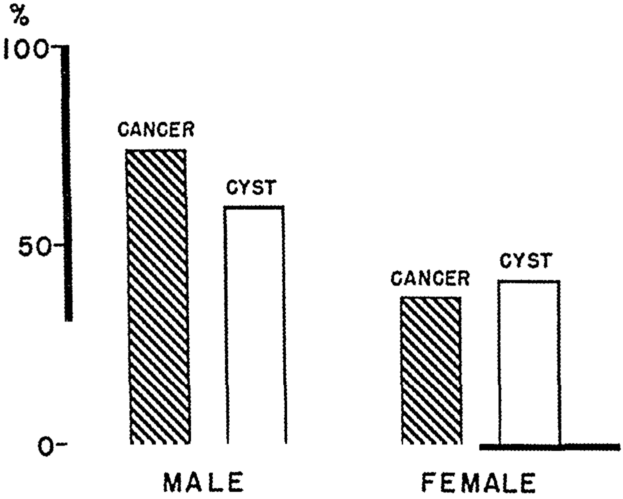
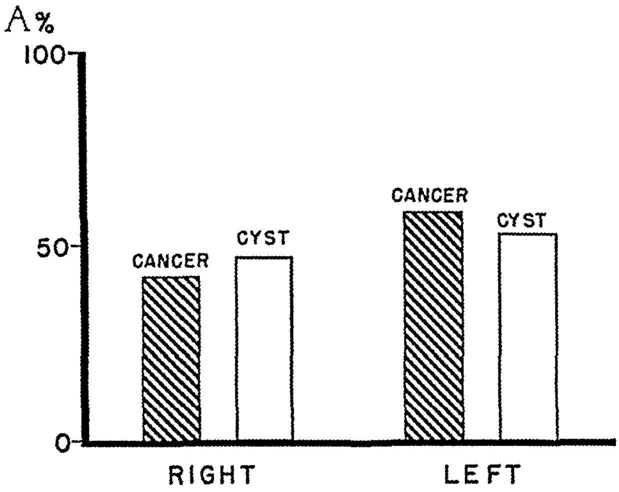


Fig. 2. Sex distribution.



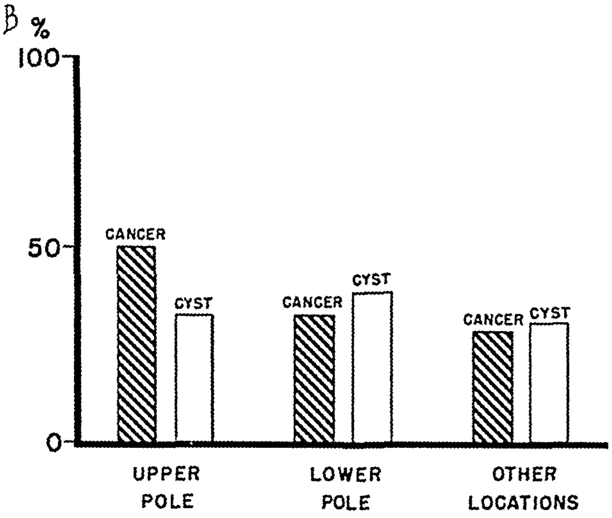


Fig. 3. *A*, laterality. *B*, location of renal mass.

local and extrarenal proved to be cysts, as did most of those which failed to produce calyceal distortion. A local, extrarenal mass was defined in this study as one originating within the kidney but whose outline protruded extrarenally beyond an otherwise relatively normal renal outline. That this type of shadow is often associated with solitary cyst was pointed out by Herbst and Vynalek, but we found that it did not exclude cancer as the diagnosis. Apparent ampu-

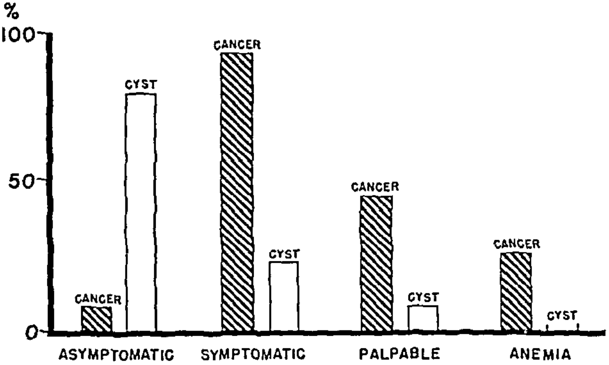


FIG 1 Clinical signs

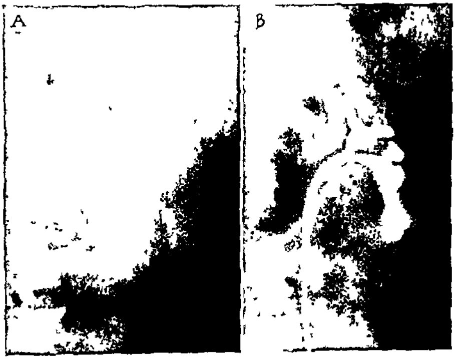


FIG 5 Deformity of lower major calyx of left kidney seen in excretory urogram of patient with solitary, serous cyst A, after retrograde dye injection B, deformed calyx is seen to be distensible

TABLE 2 *Extrarenal roentgen abnormalities*

	Tumors (36)	Cysts (47)
Axis deviation	16	13
Ureteral displacement	7	4
Changes in psoas shadow	7	0

blood counts, a chest x-ray, cholecystogram, barium enema, and upper gastrointestinal series yielded normal findings. Excretory urograms and a nephrotomogram showed an avascular, spherical mass 12 cm. in diameter in the upper pole of the left kidney. At operation this proved to be a solitary, serous cyst which was removed by one of the authors (B. G. C.). Symptoms disappeared immediately after operation and did not return during 2 years of observation.

Second, the cyst may destroy renal cortex by pressure (Herbst and Polkey; Leadbetter) or by ureteral obstruction and secondary hydronephrosis (Kretschmer).

Third, infection may occasionally occur within a cyst (Nelson and Hooper).

Fourth, reversible hypertension of the Goldblatt-Page type is occasionally the result of solitary cyst (Kreutzmann).

Fifth, small cancers occasionally occur within the walls of otherwise typical solitary cysts (Emanuel; Hepler; Youngblood). Even in a typical serous cyst, the entire wall should be carefully inspected for such a lesion. Hemorrhagic cysts are known to be associated with cancer in about one-third of the cases.

Sixth, solitary cyst may occasionally be subject to spontaneous rupture and cause serious hemorrhage, as illustrated by the following case:

Case report. A 37-year-old man experienced acute, left flank pain while lying in bed. This became more severe during the next half hour. He was admitted to the hospital in shock, with a large, tender, flank mass on the left. The pyelogram showed gross deformity and an extrarenal mass (fig. 9). At operation, performed by one of us (L. R.), a large retroperitoneal hematoma that was evacuated contained fragments of the wall of a typical serous cyst the identity of which was proved histologically.

These considerations all suggest that operative removal of the serous cyst is to the patient's advantage in the usual good risk case apart from its value in proving the absence of cancer. We believe, however, that if operative intervention is seriously contraindicated and that the renal mass can be proved typically spherical and avascular by aortograms, nephrotomograms or nephrograms (Herzan, Berry and Cross), translumbar needle puncture may be done to establish the diagnosis of solitary, serous cyst. After needle puncture, an x-ray contrast medium may be injected to delineate the lesion; and bacteriologic, cytologic and chemical study of the fluid may be carried out further to corroborate the diagnosis.

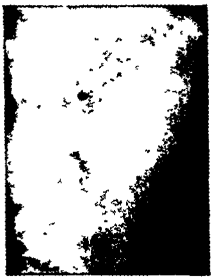


FIG. 9. Retrograde pyelogram after spontaneous rupture of solitary cyst of left kidney with exsanguinating hemorrhage.

THE JOURNAL OF UROLOGY
Vol 75 No 6 June 1956
Printed in U S A

RENAL FUNCTIONAL PATTERN IN CALCULOUS DISEASE

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Notwithstanding the increasing number of experimental and clinical works performed in recent years on the problem of renal lithiasis, the functional pattern of the kidney in this disease has received little if any attention

The present investigation was undertaken in order to explore the renal function in a selected group of patients with a history of renal or ureteral calculi

METHODS

All studies were done in the morning, 12 hours after the last meal The subjects were orally hydrated with 400 cc of light tea 1 hour before the procedure An indwelling catheter was inserted into the bladder and an intravenous infusion of 0 02 cc of a 30 per cent diodrast solution per minute was started After a 30-minute "equilibration" period, urine was collected during periods averaging 15 minutes each Venous blood samples were obtained from an antebrachial vein at the mid point of each period Simultaneous clearances of urea, endogenous creatinine and diodrast were determined

After increasing the infusion of diodrast until a plasma level of about 20 mg per cent was obtained, two periods were run for measuring the tubular mass for the excretion of diodrast

Diodrast clearance was used as indicator of renal plasma flow, glomerular filtration rate was determined from the endogenous creatinine clearance, simultaneous urea plasma clearance was also determined The tubular mass was determined for the excretion of diodrast at high plasma level

CLINICAL SUBJECTS

The subjects for this study were 10 nonhypertensive patients with one or more episodes of urinary stones, without any present evidence of urolithiasis, renal destruction or pyelocaliectasis in the excretory urogram They ranged in age from 37 to 52 years Five of them had to be operated on in order to remove the stone, the other five passed the stones spontaneously or following cystoscopic maneuvers None of them had any evidence of hypertension, cardiovascular or renal disease, except past lithiasis

RESULTS

Table 1 presents the data from each subject

Effective renal plasma flow is definitely below the normal range of plus or minus twice the standard deviation from the respective male and female means (table 2) (early)

The glomerular filtration rate falls below the normal range in 9 cases, being only in one case within the normal range

Accepted for publication January 11, 1956

TABLE 1

Case	Sex	Age	Blood Pressure	Plasma Urea	Urea Clearance	GFR	RPF	FF	Tm	II
				mg. %	*%*	*cc*	*cc*		*mg.*	
1. A. P.	♂	46	130–80	46	66	64	392	.16	32	12
2. H. D.	♂	52	120–80	45	84	70	380	.18	19	15
3. J. D.	♂	42	150–100	36	55	70	280	.25		
4. L. P.	♂	37	120–80	57	74	90	262	.34	19	14
5. J. F.	♂	48	120–70	61	66	80	270	.30	37	7
6. J. B.	♂	39	130–90	73	51	50	270	.18	21	13
7. J. D.	♂	50	140–80	35	74	55	260	.21	16	16
8. B. M.	♂	45	130–80	57	70	90	230	.41	38	8
9. L. B.	♂	47	130–80	40	100	60	220	.26	24	10
10. A. B.	♀	46	120–70	22	60	70	170	.41	17	9

TABLE 2

	Male		Female	
	Mean	σ	Mean	σ
Glomerular filtration rate (GFR)	*131*	*21.5*	*117*	*15.6*
Renal plasma flow (RPF)	697	136	594	102.4
Filtration fraction (FF)	0.19	0.02	0.20	0.03
Tm diodrast (TmD)	52	8.7	42	9.4
Irrigation index (II)	14	2.1	14	2.3

σ: Standard deviation.

The filtration fraction (glomerular filtration rate/renal plasma flow) does not follow a regular pattern, it averages 0.27; being normal in 6 cases and above the normal range in 4 cases.

Only in 2 cases Tm diodrast is within the normal range, in 8 cases it falls below.

Renal plasma flow/Tm diodrast ratio falls within the normal range in all cases.

The concentration of urea in plasma ranges from 0.22 to 0.73 g per cent.

DISCUSSION

The severe reduction of the values of renal plasma flow, glomerular filtration rate and tubular mass in the present cases is striking since none of them has hypertension, or any clinical or laboratory evidence of past or present glomerulonephritis or any other renal disease.

The increase of the filtration fraction in some of the present patients is similar to that observed almost in every case in which the renal plasma flow is reduced below 300 cc per minute.

The almost normal value of the renal plasma flow/Tm diodrast ratio is worthy of being stressed since it denotes a proportional reduction of renal irrigation and the amount of functioning tubular parenchyma.

In the absence of signs of renal destruction or urostasis due to obstruction in the excretory urogram, the possibility that the functional pattern may be the expression of the underlying cause of the calculous disease must be taken into account

A mechanical or reflex influence of stones on the kidney can be excluded since all the patients are at the time of the study free of evidence of renal or ureteral calculi for at least four months

The possibility that the described modifications of the renal functional pattern are merely coincidental with the calculous disease cannot be ruled out, but it still remains as an uncontroversial fact, as far as our observations are concerned, that in every case of past history of urinary lithiasis the renal functional exploration revealed such modifications

SUMMARY

The renal functional pattern in 10 cases of renal calculous disease is described

Notwithstanding the absence of hypertension or evidence of present renal disease, renal plasma flow, glomerular filtration rate and Tm diodrast were severely reduced

These observations suggest the possibility that the deep alteration of the renal function observed in calculous disease may depend on the underlying cause of the lithiasis

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REFERENCE

EARLY, D. P : Am. J. Med , 9: 78, 1950

THE JOURNAL OF UROLOGY
Vol. 75, No. 6, June 1956
Printed in U.S.A.

ELECTRON MICROSCOPY OF A CYSTINE UROLITH

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While x-ray diffraction[1, 2] has proved a useful and rewarding tool in the study of the structure of kidney calculi (analysis of the stones is done by this method on a routine basis), electron microscopy has not yielded results as readily. It is of interest to study the structure of uroliths by electron microscope techniques because of what may be learned about the manner in which the stones are constructed, particularly in the neighborhood of the core, at the interface of the layered areas; and in stones where x-ray diffraction has indicated a composite of crystalline materials. From such studies some insight into the mechanism of stone formation itself may be gained.

The principal difficulty in the electron microscopy is to develop a method for replicating the surfaces of the calculi so that their structures can be examined by application of the high resolution afforded by the microscope. The stones are difficult to replicate because they are often of soft or porous structure. Many times, they are so insoluble in usual solvents that ordinary replicating methods are impossible. Crushed fragments yield no significant information.

Therefore, although many other replicating methods were attempted, none yielded reliable results until carbon replicas were employed. The adaptation of the carbon replication technique[3] to the problem resulted in these first electron micrographs of the fine structure of a kidney calculus. The present paper describes the procedures and illustrates the results with a urolith of cystine. This particular stone was examined earlier by x-ray diffraction and chemical means and reported in footnote 1. It is of special interest because, contrary to usual observation of cystine stone, it was found to be opaque to x-rays[4] and could not be cut easily with a knife.[5] Prien and Frondel[6] describe cystine calculi as very soft unless they are densely granular. This stone did not seem to be granular but was quite hard. It was hoped that some of these facts might be reconciled by electron microscopic observation of the fine structures. By both diffraction and chemical methods the stone was judged to be a very high purity of cystine. Clinical data concerning the patient from whom it was taken are contained in footnote 1. Electron microscopically the stone was used because it was large enough (27 by 19 by 13 mm.), to make handling less of a problem, because cystine is relatively easily dissolved

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Accepted for publication January 26, 1956.

[1] Parsons, Jonathan: Radiopaque renal calculus identified as cystine by x-ray diffraction. Radiology, **58:** 878-80, 1952.

[2] Parsons, Jonathan: Zinc phosphate identified as a constituent of urinary calculi. Science, **118:** 217-218, 1953.

[3] Bradley, D. E.: A high-resolution evaporated-carbon replica technique for the electron microscope. J. Institute of Metals, **83:** 35-38, 1954-5.

[4] Kerr, H. D. and Gillies, C. L.: The Urinary Tract: A Handbook of Roentgen Diagnosis. Chicago: Year Book Publishers, 1944.

[5] Michels, A. G. and Engel, W. J.: Cystinuria and cystine calculi. Cleveland Clinic Quart., **17:** 80-88, 1950.

[6] Prien, E. L. and Frondel, C.: Studies in urolithiasis; composition of urinary calculi. J. Urol., **57:** 949-994, 1947.

in KOH and because it (the stone) was relatively compact, hard and readily replicated

The cystine of this stone was identified by x ray diffraction as *l*-cystine, which has an hexagonal trapezohedral structure with crystals occurring as tablets with perfect basal cleavage along the (0001) planes

EXPERIMENTAL METHODS

To prepare replicas for electron microscopy, the calculus was split and a section removed for polishing and etching in KOH The section was broken into pieces, each of which was labelled as to location and then set individually within an evaporator,* so that the desired areas of the stones would receive the direct carbon film The carbon arc was arranged directly above the samples and was heated and evaporated by the usual techniques Figure 1 is a schematic drawing which shows the experimental arrangement It was found that carbon deposited upon all surfaces to some extent except the bottom and appreciably thick and useful films were retrievable also from the sides although the carbon film was obviously thickest upon that surface facing the arc Consequently, it was possible to obtain carbon replicas of more than one side of a section at a time and to study the surface of any plane plus the surface of a plane perpendicular to it Although replicas of the stone were taken from six different locations and from two different layers, parallel and perpendicular to the plane there were no reproducible or recognizable differences in the morphology of the various areas The same appearances were reported for each set of replicas and it was concluded that the composition was uniform throughout The micrographs which are shown are chosen for the *type* of *structure they represent, but are representative* for all sections of the stone

Some discussion of the experimental method is necessary for a proper interpretation of the image intensities in the micrographs It should be remembered that carbon replicas give excellent contrast and that slight differences in thickness give considerable difference in image intensities Thus many of the micrographs give the clarity of a line drawing The micrographs are positives and wherever the image is a lighter density the carbon film is thinner The micrographs give an impression of perspective in three dimensions because of the high contrast, and the foreshortened areas are particularly dark in the micrographs because of the effectively thicker targets offered to the electrons by the projected replica volumes Sloping areas which are slanted less abruptly, appear lighter than those at more acute angles This is illustrated in figure 2 which shows a typical surface *in cross section at A* At *B* the surface is shown coated with carbon deposited normally upon it In *C* the cystine stone has been dissolved away leaving the replica alone Although approximately the same thickness of carbon has been deposited everywhere, the slopes present effectively thicker targets with more electron scattering power In the electron optical image, therefore, the slopes are less intense and the flat planes brighter In the negative image, *D*, consequently,

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* Optical Film Engineering Company, Inc , Philadelphia 33, Pennsylvania Model No SC 3

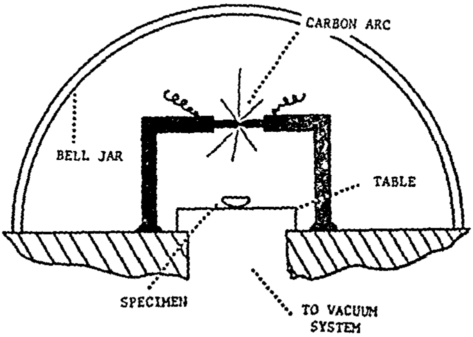

FIG. 1. Schematic drawing of experimental arrangement for depositing carbon film upon specimen surface.

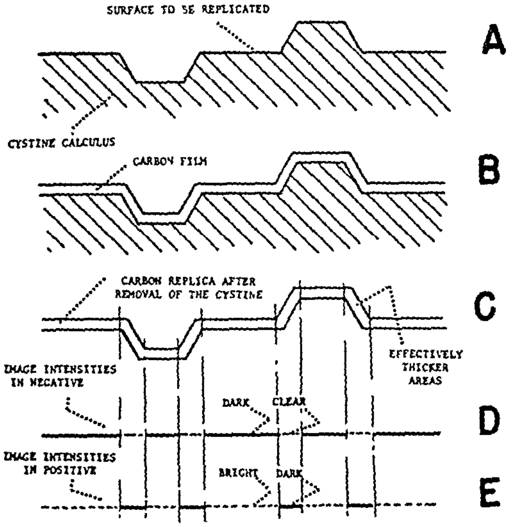
SURFACE TO BE REPLICATED
A
CYSTINE CALCULUS
CARBON FILM
B
CARBON REPLICA AFTER REMOVAL OF THE CYSTINE
C
EFFECTIVELY THICKER AREAS
IMAGE INTENSITIES IN NEGATIVE
DARK
CLEAR
D
IMAGE INTENSITIES IN POSITIVE
BRIGHT
DARK
E

FIG. 2. Schematic representation of manufacture of carbon replica: *A*, cross-section of original cystine sample. *B*, cystine surface coated with uniform deposit of carbon. *C*, carbon replica after removal of cystine. *D*, image intensities on negative plate obtained by electron microscopy and *E*, image intensities on positive micrograph.

the slopes are light and the flat planes dark: and in the final positive prints, *E*, the slopes are relatively dark and the flat planes are bright.

The *very* light areas in some micrographs are due to a shadow casting effect of the carbon deposit. The carbon source is relatively large (2 or 3 mm.), and it is relatively close (15 cm.), to the depositing surfaces and therefore with certain geometry it is possible for certain areas to be more or less protected from the direct path of the carbon vapor and for *shadows* to be formed. (A shadow under these circumstances is a relative absence of carbon.) These shadows are particularly present in figure 4, *A* (arrow).

The micrographs were all taken with an EMU-2B* instrument, with and without an objective diaphragm. Wherever a diaphragm was used it had a diameter of 25 microns. The original plates were taken at the low magnification of 1680× and enlarged optically to 5000× and 10,000× for publication.

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* Manufactured by Radio Corporation of America.

OBSERVATIONS

In almost every micrographed field the compact, well constructed nature of the stone was especially striking. Porous places were not seen and granular areas were exceedingly rare. The nature of one of the few granular areas observed is given in figure 3, A. The tiny crystals seen are met very infrequently in the stone and are probably a function of what might be called the few porous or granular locations. In general, this section is parallel to the (0001) plane, the characteristic

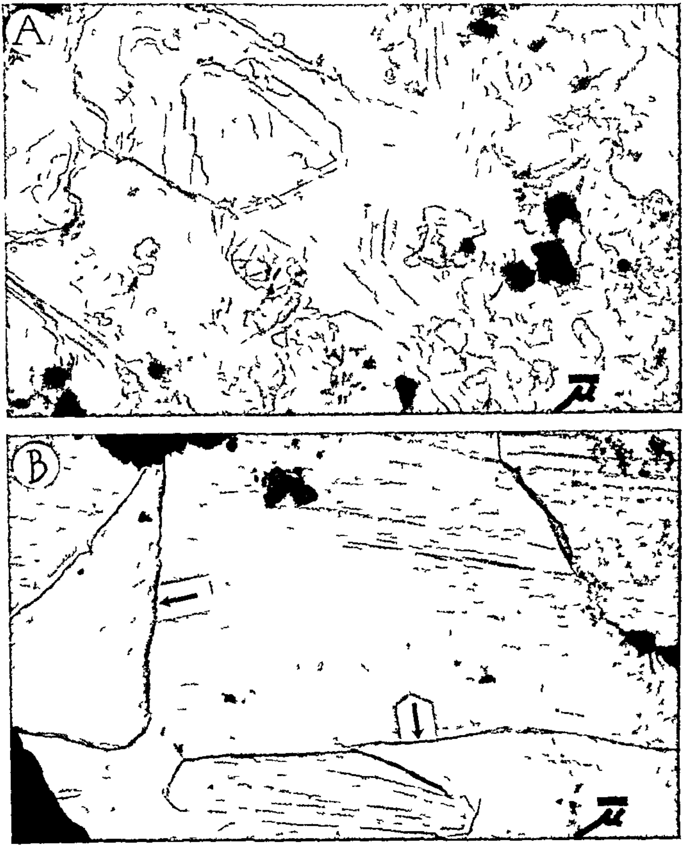

Fig. 3. Carbon replicas of cystine urolith, ×5 000. *A*, to show small granular material infrequently observed. *B*, to show several 'grains' or crystalline areas meeting in one location.

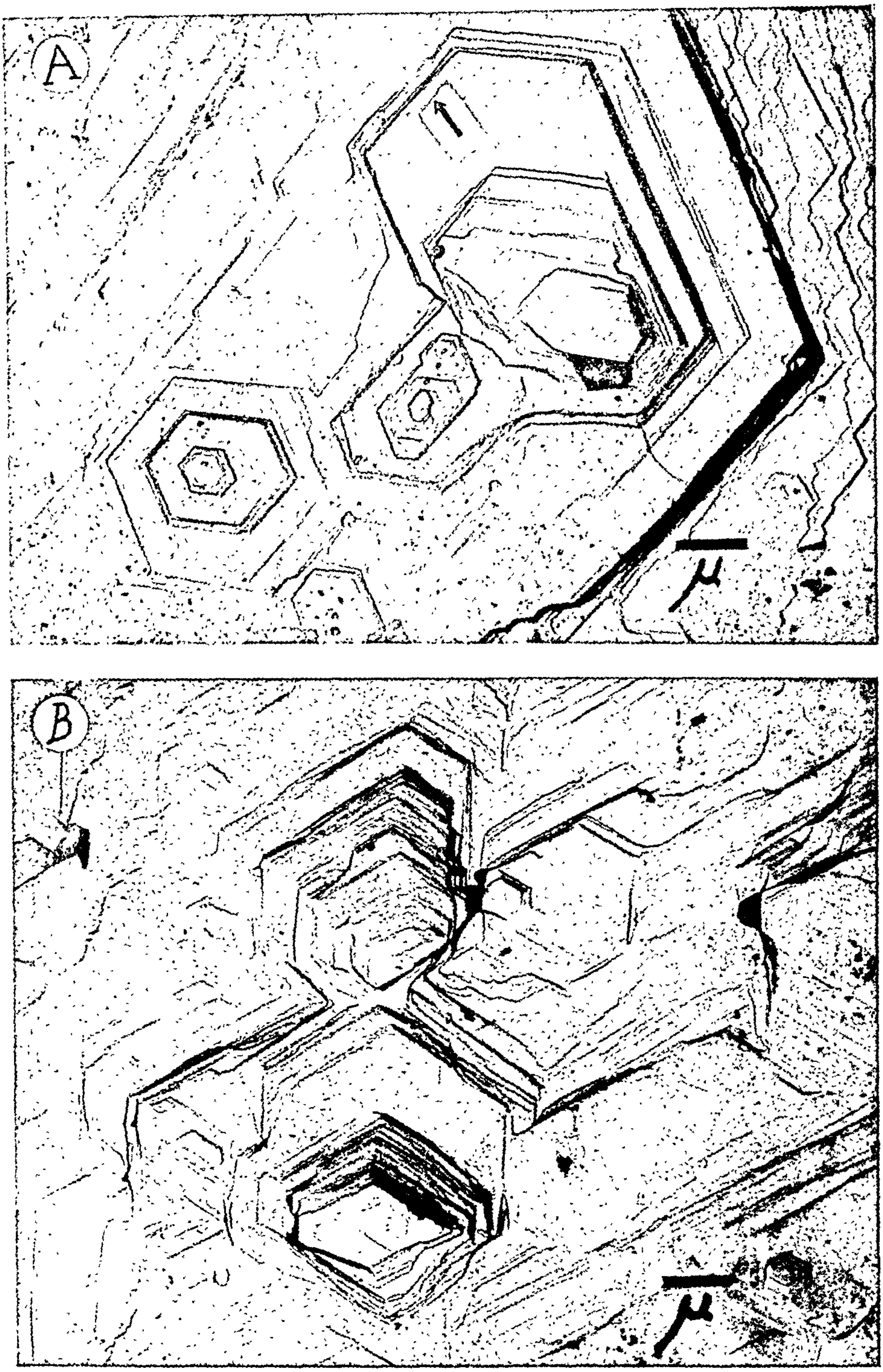

FIG. 4. Carbon replicas of cystine urolith, ×10,000, parallel to (0001) plane, showing hexagonal depressions and piles of hexagonal tablets.

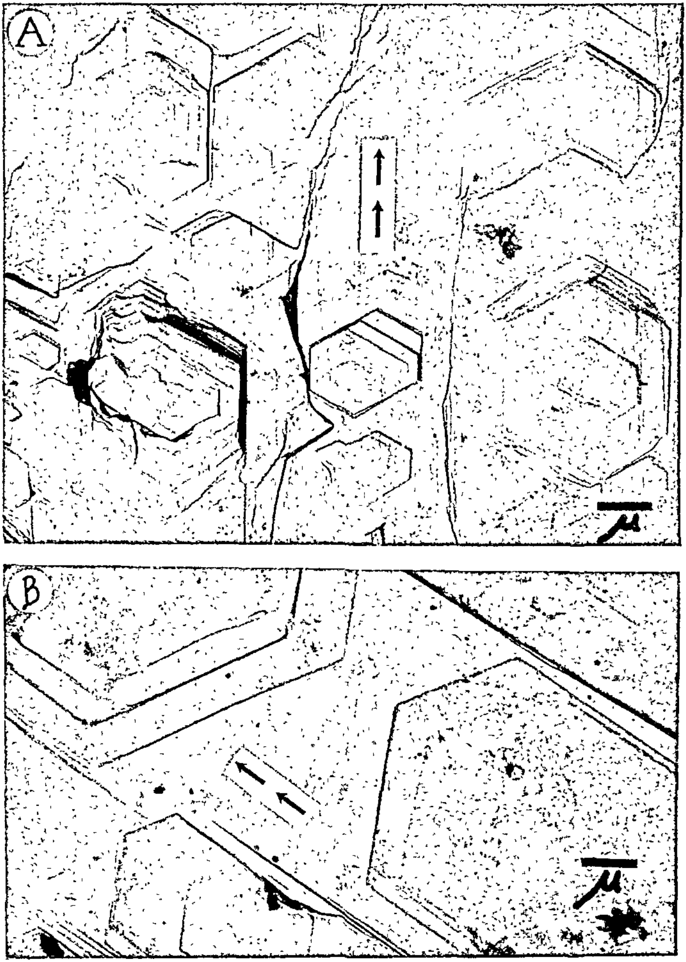

FIG. 5. Carbon replicas of a cystine urolith, ×10,000, parallel to (0001) basal cleavage plane.

120° angles of the hexagon are visible everywhere, but the structure appears a little less perfect than in most sections to follow. The very dark areas are probably cystine material not removed from the carbon film by the KOH etching. There is *apparently a differential etching by KOH over the surface of the cystine which results in excellent rendition of the basic structures.*

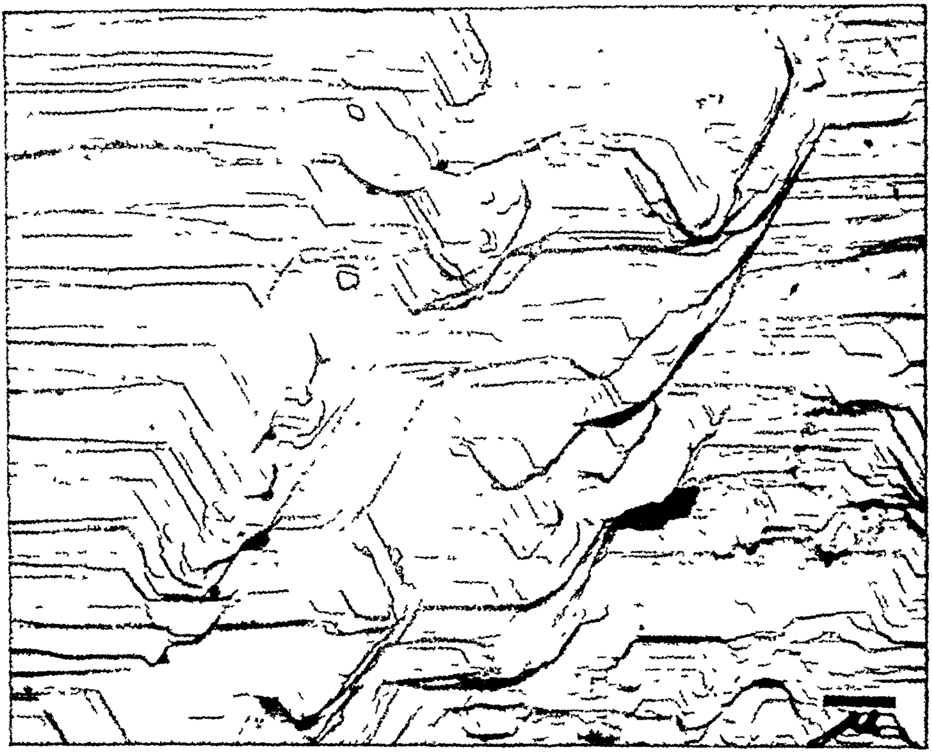

FIG. 6. Carbon replica of cystine urolith ×10,000, showing field with (0001) planes tipped slightly to plane of micrograph

Figure 3, *B* is included to show at relatively low magnification that several *grains* or crystals may be arranged closely together in many locations. In the figure are seven grains in close juxtaposition. The stone is therefore an arrangement of close-packed small crystalline units, with very little space, if any, between them. The dark, linear areas (arrows) represent narrow fissures between these grains. The lighter linear areas lying approximately parallel within the grains are narrow steps, indicating the cleavage planes within the crystals. *Within a grain* these have a constant direction which varies from grain to grain.

Two examples of structures in the (0001) plane are given in figure 4. The general appearance of hexagonal plates piled upon each other is similar to that observed in the light microscope[7] except that finer detail is resolved here. Hexagonal depressions are also noted. The hexagons are discrete and there is no spiralling at the edges of the piles or depressions, such as has been reported for etched germanium[8] crystal surfaces and for other materials.[9] The exceedingly compact nature of the calculus is observed again. Further examples of structure parallel to the cleavage plane is shown in figure 5. Figure 5, *A* has mostly small, hexagonal areas all directed more or less parallel to the arrow. Figure 5, *B* shows much

[7] Hawk, P B , Oser, B L. and Summerson, W. H : Practical Physiological Chemistry. Philadelphia The Blakiston Co , 1951, p 127.

[8] Ellis S G Dislocations in germanium J. App Phys., 26: 1140-1146, 1955

[9] Amelinckx, S Growth features on crystals of long chain compounds I Acta Cryst., 8: 530-537 1955

larger cleavage planes, not so deeply etched, all arranged again in a constant direction.

The rest of the figures show fields wherein the cleavage planes are oriented at greater and greater slopes to the plane of the micrographs. They demonstrate conclusively the extremely compact nature of the stone's structure and explain its opacity for x-rays and its hardness. In figure 6 the planes are only slightly tipped and the flat areas are still predominant in the field. There are no complete hexagons but there are many lines with angles of 120 degrees between them. In figures 7, *A*, 7, *B* and 8, *A* are fields with the cleavage planes tipped even further until the edges of the cleavage planes rather than their flat surfaces are becoming

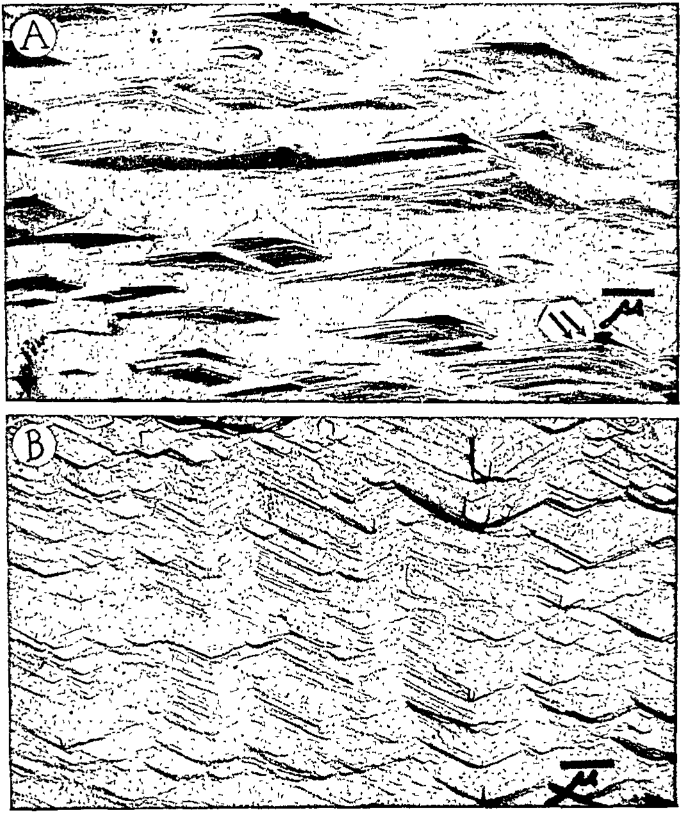

FIG. 7. Carbon replicas of cystine urolith ×10,000, showing fields tipped with (0001) plane about 45 degrees to plane of micrograph.

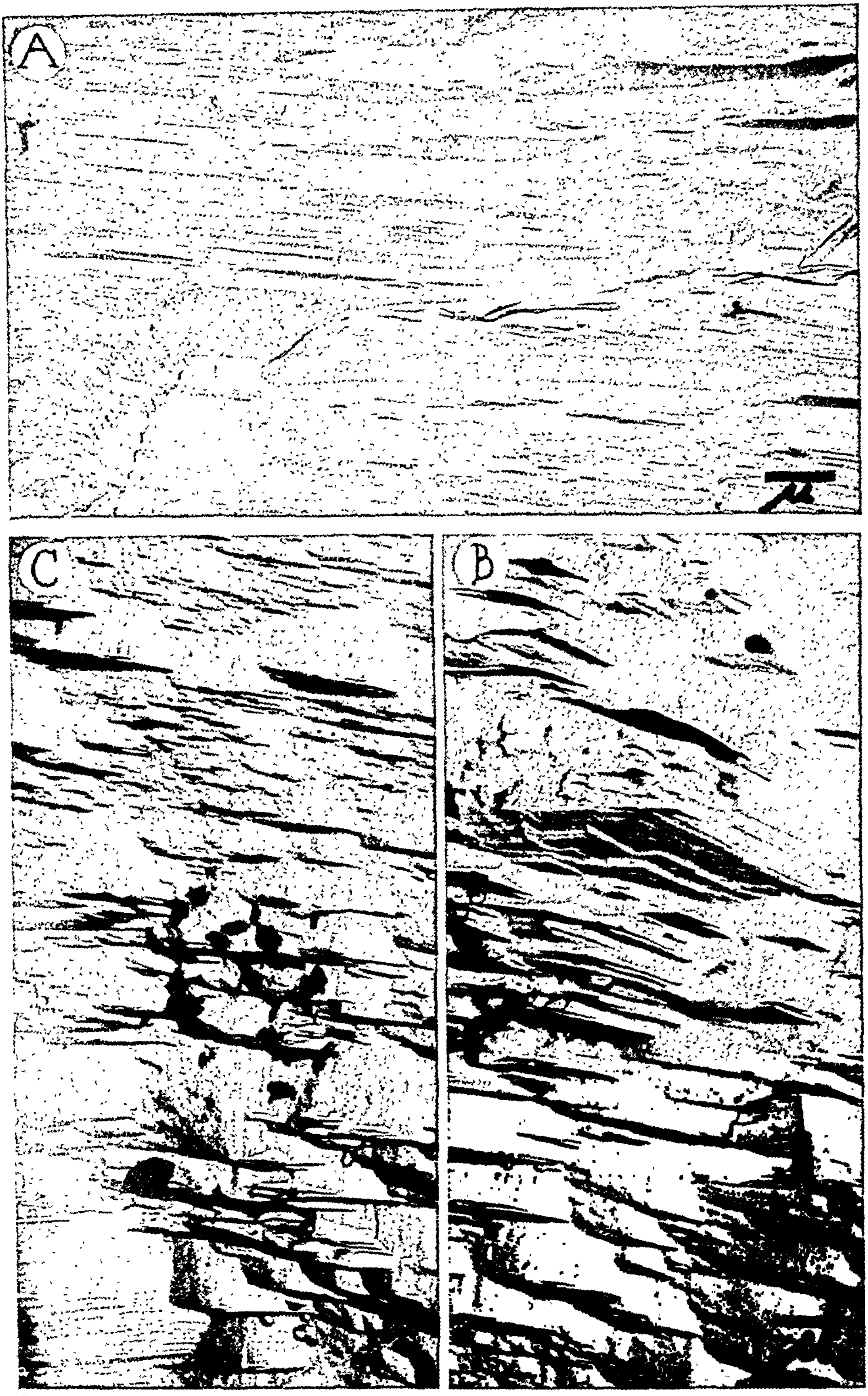

FIG. 8. Carbon replicas of a cystine urolith ×10,000, showing in *A* a field tipped with (0001) plane about 60 degrees to plane of micrograph, and in *B* and *C* fields tipped with (0001) plane approximately perpendicular to plane of micrographs.

predominant in the micrographs. In figure 7, *A* the tips of the hexagonal tablets have been etched or broken to protrude so far that they throw long shadows (light triangles). The planar nature is still visible everywhere. In one location (double arrow) the complete layers come to an 120° angle point and some structure perpendicular to them in the tablet can be seen.

In figure 7, *B* the perpendicular structure is not seen, the planes have been more uniformly etched than in figure 7, *A* and lie in layers of close packing, side by side like the teeth of a saw. In figure 8, *A* a good example of the long, close packed planes is seen. In figures 8 *B* and *C* are examples wherein the cleavage planes are almost perfectly perpendicular to the plane of the micrographs. Everywhere, the very compact nature of the packing is clearly visible. The fine structure at right angles to the cleavage planes is again visible but has a contrast much inferior to that in the direction of the cleavage planes. The individual platelets have a minimum measurable thickness of about 30 mμ.* and are separated by a minimum distance of about 10 mμ. Tablets as thick as one micron are seen.

DISCUSSION

From this work it may be concluded that the carbon replica method can be used productively in the electron microscopy of uroliths. It has shown about cystine calculi in particular that where they are opaque to x-rays and hard, these properties are due to particularly efficient packing of the cystine tablets into the macroscopic stone. The only granular, or porous areas in this particular stone might be designated as those areas where the structures were broken and tiny as in figure 3, *A*. There did not seem to be any overt changes in morphology from location to location in this stone, and no core structure could be determined as such. There was no visible evidence of colloid, the stone being a result of a crystal formation from solution. In stones of other genesis it might be that colloidal structures would be demonstrable by the electron microscope.

SUMMARY

A method for studying the structure of uroliths by electron microscopy of carbon replicas is introduced. The method is illustrated by the first electron micrographs taken of a cystine calculus.

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* A millimicron (mμ.) equals 10^{-7} centimeters.

THE JOURNAL OF UROLOGY
Vol. 75, No. 6, June 1956
Printed in U.S.A.

EXPERIENCES WITH THE ILEAL CONDUIT IN URINARY DIVERSION

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Encouraging reports in the medical literature concerning the use of an isolated segment of terminal ileum offers a new approach to the problem of urinary tract diversion. The results and impressions of this procedure in a series of patients are presented. The patients had a diversity of pathological lesions.

Diversion of the urinary stream will always constitute a major urological problem. Certain limitations have attended all approaches to this problem. Obstruction, reflux, infection and electrolyte imbalance are hazards following bilateral ureterosigmoidostomy. Cutaneous ureterostomy requires much paraphernalia. Unilateral renal exclusion has been suggested to minimize postoperative care. Stricture of the stoma and ureter is a constant threat. An indwelling ureteral catheter is a foreign body and may aggravate infection or cause calculus disease. Transplantation of the ureters to a rectosigmoid pouch has been advocated. This use of the rectum as an urinary reservoir with voluntary control must be associated with a proximal colostomy without voluntary control. Perineal sigmoidostomy, utilizing the rectal sphincter for fecal control as suggested by Lowsley, may be a solution. Use of the ileocecal pouch as a substitute bladder offers much promise.

Diversion of the urinary stream to an isolated ileal segment seemed ideal for several reasons. Continuous contamination by the fecal stream was avoided. The fecal current was preserved and no colostomy was needed. Little or no absorption of metabolites or electrolytes into the circulation was found because the ileal segment was merely a conduit. No reservoir existed to allow constant exposure of intestinal mucosa to urine. Reflux of infected secretions was not a danger because the hydrostatic pressure gradient could not be reversed. Preservation of the ureteral blood supply enhanced healing without stricture. Ureteral blood supply was maintained because only short segments of the ureteral bed were disturbed. The ileal segment was fixed to the posterior peritoneum where the ureters emerged from the retroperitoneum.

Preoperative preparation for ileal shunt surgery was simple by comparison to the exhausting routine needed to ready the large bowel for ureterointestinal anastomosis. The fecal stream is liquid in the ileal segment. The bacterial count is less in the ileal segment than in the colon.

A high protein, low residue diet supplemented with vitamins was used. Sulfasuxidine, 12 gm. each day, was given for 5 days. Repeated enemas were given the morning of surgery until the return flow was clear. Wangensteen drainage was started the night before surgery. This routine has always yielded a well-prepared ileum.

Read at annual meeting, North Central Section of American Urological Association, Chicago, Ill. September 29-October 1, 1955.

The usual attention to the hemogram, a positive nitrogen balance, and the cardiovascular status is necessary as in all major surgery

The surgical technique as described by Bricker has been followed The ileocecal segment has been avoided because of the vascular limitations in this area A sufficient length of ileum was used to establish a conduit from the cutaneous ostium in the lower right abdominal quadrant to the promontory of the sacrum End to end ileo ileostomy and anastomosis of both ureters to the conduit complete the operation Minimal segments of ureter are isolated All techniques of ureteral anastomosis have been used The musoca-to mucosa method was preferred Splinting ureteral catheters were used to insure against early postoperative edema and obstruction at the anastomotic site

Postoperative management has presented no unusual problems The threat of abdominal distension has required the extended use of the Wangensteen drainage Mucus, which issues from the ileostomy, has soiled the dressings The indwelling plastic ureteral catheters have become plugged Removal of the catheter is preferable to overzealous attempts at irrigation Blood chemistry determinations have shown no abnormal deviations Use of the ileostomy bag has been delayed until healing has become established

CASE REPORTS

Case 1 Mr McL , a white man 43 years of age, had extensive carcinoma of the bladder The ileal shunt was performed as a palliative procedure The diversion of the urine was effected and the ileal conduit functioned perfectly The patient died 2 months after operation with carcinomatosis The blood electrolytes remained normal No autopsy examination was permitted

Case 2 Mr W W , a white man 51 years of age, had extensive carcinoma of the bladder The ileal shunt was performed and functioned well A perineo abdominal cystectomy and prostatovesiculectomy were effected later No renal symptoms have been noted Examination 9 months after cystectomy revealed evidence of carcinoma Figure 1, *A* is a preoperative excretory urogram The left kidney did not visualize The left ureter was found to be remarkably dilated at surgery Both ureters were anastomosed to the ileal conduit Figure 1, *B* is an excretory urogram taken 2 months after surgery The left kidney fails to visualize Minimal hydronephrosis is noted on the right side Figure 1, *C* is an excretory urogram taken 6 months after the construction of the ileal conduit and 3 months after cystectomy Essentially normal morphology of the right kidney and ureter is noted

Case 3 Mr F S , a white man 74 years of age, had extensive carcinoma of the bladder He died 3 days after the ileal shunt was constructed The cause of death was bronchopneumonia No urinary leakage or obstructive lesion was found at autopsy No pyelonephritis was found No peritonitis was found Figure 2 depicts the gross autopsy specimen The stumps of the ureters are seen to protrude into the lumen of the opened ileal segment All anastomotic lines were tight but there seemed to be no evidence of the normal healing tendency at 72 hours postoperatively

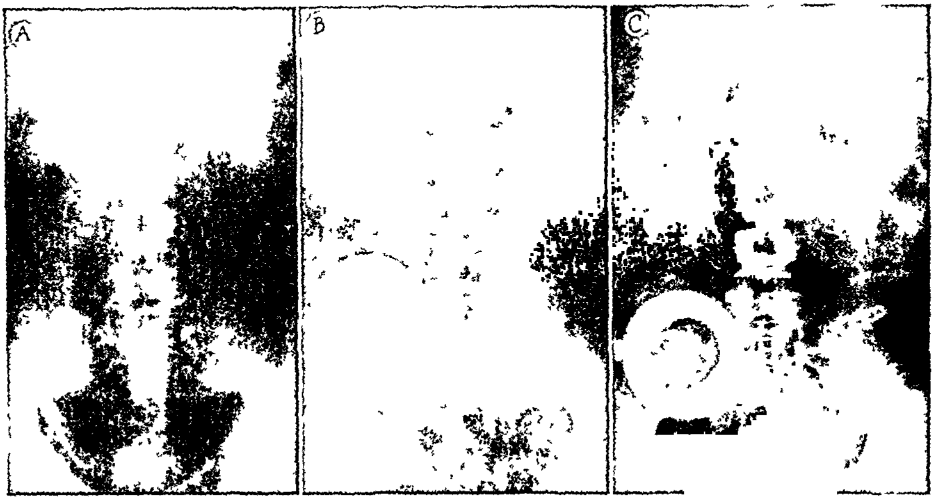

FIG. 1. Case 2. *A*, preoperative excretory urogram demonstrates normal right kidney and ureter. Left kidney fails to visualize *B*, excretory urogram, 2 months after surgery, shows minimal right hydronephrosis Left kidney fails to visualize. *C*, excretory urogram, 2 months after surgery, shows normal right renal and ureteral morphology.

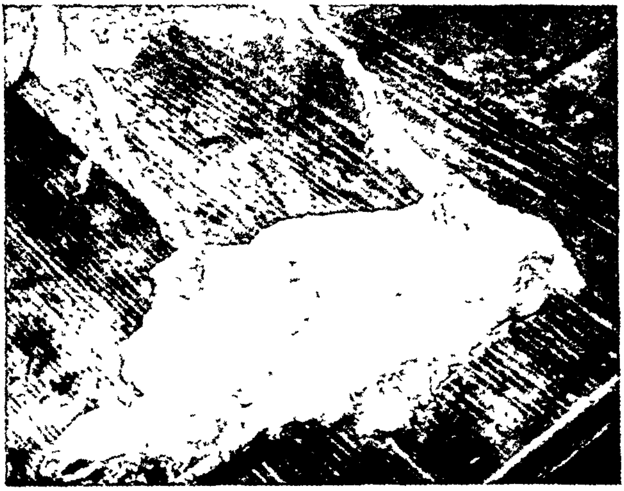

FIG 2. Case 3 Autopsy specimen includes opened ileal segment and both ureters. Protruding and unobstructed ureteral stump is visible.

Case 4. Mrs. F. A., a 26-year-old Negress, had irreparable x-ray and radium injury to the bladder incurred in treatment of carcinoma of the cervix. Radiation had caused complete necrosis of the trigone and proximal two-thirds of the urethra The ileal shunt has provided an excellent method for urinary diversion. Figure 3, *A* is a preoperative excretory urogram which demonstrates bilateral hydronephrosis. Figure 3, *B* is an excretory urogram taken 1 month after diversion of the urine to the ileal segment. The hydronephrosis has become aggravated. Subjectively, the patient was improved. Figure 3, *C* demonstrates the persistence of the hydronephrosis 2 months after surgery. Figure 3, *D* is an excretory urogram taken 5 months after diversion. The hydronephrosis has improved. Figure 4 shows sustained improvement 13 months after surgery. The

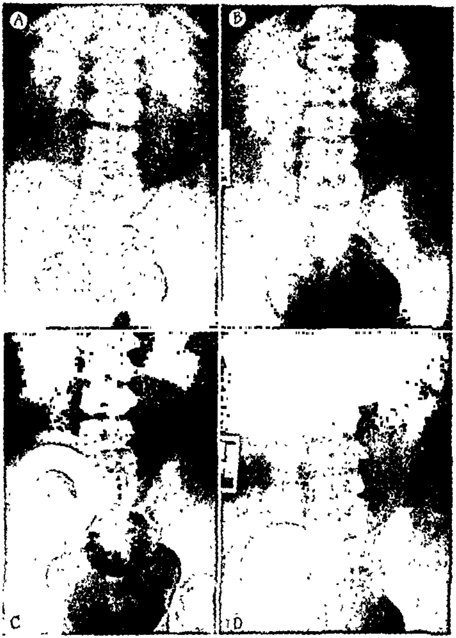

FIG. 3. Case 4. *A*, excretory urogram demonstrates preoperative bilateral hydronephrosis. *B*, excretory urogram, 1 month after surgery, shows increase of hydronephrosis. *C*, excretory urogram, 2 months after surgery, shows continued hydronephrosis. *D*, excretory urogram, 5 months after surgery, shows improved morphology of both renal pelves.

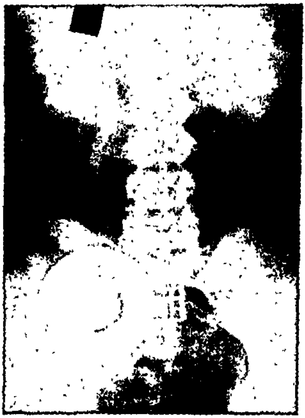

FIG. 4. Case 4 Excretory urogram, 13 months after surgery, shows sustained improvement in renal morphology.

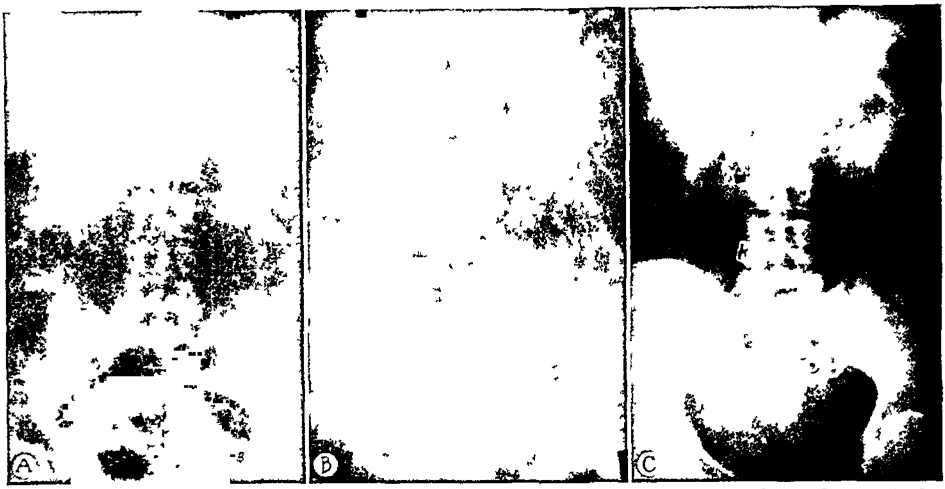

FIG. 5. Case 8. *A*, preoperative excretory urogram demonstrates normal renal morphology. *B*, excretory urogram, 1 month after surgery, shows normal renal morphology. *C*, excretory urogram, 5 months after surgery, shows hydronephrosis which was found to be caused by carcinoma. Anastomoses were patent.

patient remains well 1 year after operation. Blood chemistry values remain normal.

Case 5. Mrs. M. T., a Negress 49 years of age, had far-advanced carcinoma of the cervix, which involved the urinary bladder secondarily. The patient has been reasonably comfortable since the ileal shunt was performed 1 year ago. Blood chemistry values remain normal.

Case 6. Mrs. K. F., a white woman 50 years of age, had advanced carcinoma of the urethra and vagina. The ileal shunt was entirely successful. Renal function remained normal. The patient died 9 months after surgery of carcinomatosis. No autopsy was permitted.

Case 7. Mr. P. C., a 50-year-old white man, had extensive carcinoma of the urinary bladder. The ileal shunt was constructed and urine drained well. The ileal stoma became necrotic and sloughed one week after surgery. Urine drained from a fistula at the site of the ileostomy. Inanition became more marked and the patient died three weeks after surgery. Autopsy revealed well-healed anastomoses with no evidence of obstruction. No peritonitis was found.

Case 8. Mrs. A. C., a 65-year-old Negress, had extensive carcinoma of the bladder. The ileal shunt was constructed and extensive perivesical extension of the tumor was noted. The patient was comfortable and managed the ileostomy with ease. She died 6 months after surgery of carcinomatosis. Blood chemistry values remained normal. She had no episodes of sepsis. Figure 5, *A* is a preoperative excretory urogram. Figure 5, *B* is an excretory urogram taken 1 month after construction of the ileal conduit. No hydronephrosis was noted. Figure 5, *C* is an excretory urogram taken 5 months after surgery. Early bilateral hydronephrosis is noted. The obstruction was found to be due to carcinoma and not to any obstructive lesion at the site of the anastomosis. Figure 6 is a photograph of the autopsy specimen which shows the block of carcinomatous tissues surrounding the ileal segment. The renal parenchyma is well preserved. Figure 7 demon-

FIG 6 Case 8 Autopsy specimen Note ileal segment in block of carcinomatous tissue

FIG 7 Case 8 Autopsy specimen Ileal segment has been opened and anastomotic sites are demonstrated Mucosa to mucosa technique on left Pull through technique on right

strates the sites of ureteral anastomosis The left anastomosis was constructed by a mucosa to mucosa technique The right anastomosis was a simple pull through Neither ostium was obstructed Carcinomatous tissues occluded the ureters

Case 9 Mr R J , a 51-year old white man, had a pelvic exenteration performed because of carcinoma of the large bowel An ileal conduit was constructed

FIG. 11. Case 13. Ileal stoma

FIG 12 Case 13 Bag receptacle in place

has been able to dispense with the protective undergarments. There has been no change from the preoperative bowel habit. Alternating bouts of diarrhea and constipation constitute a difficult problem in bowel management. The ileal conduit functions perfectly. She is immeasurably improved by the urinary diversion Figure 10, *A* is a preoperative excretory urogram. An indwelling bag catheter is noted in the bladder. An excretory urogram, taken 1 month after surgery, demonstrates minimal hydronephrosis (fig. 10, *B*). Figure 11 demonstrates the ileal stoma. Figure 12 demonstrates the bag in place.

Table 1 is a summary of the pathology, the complications, and the result of urinary diversion by the ileal loop.

TABLE 1 *Urinary diversion by ileal loop*

Name	Sex	Age	Primary Condition	Duration of Life After Ileal Shunt	Complications of Ileal Shunt	*Cause of Death*	Autopsy Findings
Mc L	Male	43	Ca bladder	2 mos Died	None	Carcinomatosis	
Wm M	Male	51	Ca bladder cystectomy	Living and well 9 mos	None		
F S	Male	74	Ca bladder	3 days Died	None	Broncho-pneumonia	No urinary leakage or obstruction
F A	Female	26	Radium and x ray necrosis of entire bladder base	Living and well 1 yr	None		
M T	Female	49	Bladder involvement by ca cervix	Living 1 yr Ca present	None		
K F	Female	50	Ca of vagina and urethra	9 mos Died	None	Carcinomatosis	
P C	Male	50	Ca bladder	3 wks Died	Slough of ileal stoma	Inanition	No leakage or obstruction of ureters
A C	Female	65	Ca bladder	6 mos Died	None	Carcinomatosis	Anastomoses normal
R J	Male	51	Ca large bowel Pelvic exenteration	Living Ca present 16 mos	None		
L L	Female	56	Ca cervix Lobectomy for metastasis Pelvic exenteration	Living and well No ca detectable, 16 months	None		
M G	Male	54	Ca bladder	Living Ca present, 6 mos	Hematuria Non visualizing rt kidney		
F S	Male	69	Ca bladder	5 mos Died	Slough of stoma and urinary fistula of paramedian incision	Carcinomatosis	
P K	Female	21	Neurogenic bladder Complete incontinence	Living and well 7 mos	None		

CONCLUSION

Urinary diversion by isolated ileal loop is an acceptable procedure because of the simplicity for the operating surgeon and the relative innocuous preoperative and postoperative course for the patient. The merit of this system of urinary diversion lies in the lack of fecal contamination, the low incidence of scarring and hydronephrotic renal disease, and the absence of appreciable electrolyte imbalance. A reasonably good state of nutrition is essential, as in all surgery, to insure a good functional result. Poor healing occurred in the poor risk patients. An apparatus to collect the constantly draining urine is a handicap to be assumed.

SUMMARY

The advantages and disadvantages of the ileal conduit method of urinary diversion have been noted in a small series of patients.

We gratefully acknowledge the enthusiastic co-operation given to us in this work by Drs. John Reynolds, Raymond Firfer and Thomas Samuels.

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THE JOURNAL OF UROLOGY
Vol 75, No 6 June 1956
Printed in U S A

URINARY INCONTINENCE IN LERICHE SYNDROME TREATMENT BY EXCISION OF OCCLUDED ABDOMINAL AORTA AND COMMON ILIAC ARTERIES AND REPLACEMENT WITH HOMOGRAFT

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Review of the literature reveals no reports of urinary incontinence as a symptom of Leriche syndrome or of treatment of urinary incontinence by arterial grafting This is a report of successful treatment of Leriche syndrome with urinary incontinence in a female by excision of the occluded abdominal aorta (below the renal arteries) and common iliac arteries, and replacement of the resected aorta and its bifurcation branches with a lypholized homograft

CASE REPORT

Mrs F J, a 44-year-old-white woman, presented herself with the chief complaints of hip pains, cramps and weakness of the lower extremities, and urinary incontinence

About 5 years previously she had first noted cramping and fatigue of her lower extremities on exercise, relieved by rest, which symptoms had progressively become worse Pains developed in her back, hips and pelvis Her legs felt cold and numb Urinary incontinence, which developed in 1952, had been progressive She wore a pad at all times, which was always wet, and which she changed numerous times day and night When she would get up from a lying or sitting position, urine would "gush" from her She seldom had any urine to pass voluntarily

All previous therapy, medical and surgical, had been ineffective Bilateral lumbar sympathectomy with removal of the second and third lumbar ganglia on both sides had been performed in April 1953, and the operator at that time had palpated the aorta, which he described as a hard, rigid tube X-rays at that time had revealed calcification of the aortic arch and extensive calcification of the abdominal aorta and its bifurcation

She was treated for the urinary incontinence without benefit by a competent urologist by repeated periodic dilatations In December 1954 surgical repair of a cystocele and plication of the urethra had resulted in immediate control of the incontinence, but within a period of 2 weeks this condition had returned to its preoperative status

In addition to the bilateral lumbar sympathectomy and cystocele repair and urethral plication, her past surgical history included a bilateral salpingo-oophorectomy, approximately 20 years previously, and a hysterectomy in 1943

Physical examination revealed operative scars of her previous surgical procedures No pulsations of the abdominal aorta, or femoral, popliteal, posterior tibial or dorsalis pedis arteries in either extremity could be elicited on palpation Blood pressure, 160/75 in both arms, was absent in the lower extremities There

Accepted for publication December 21, 1955

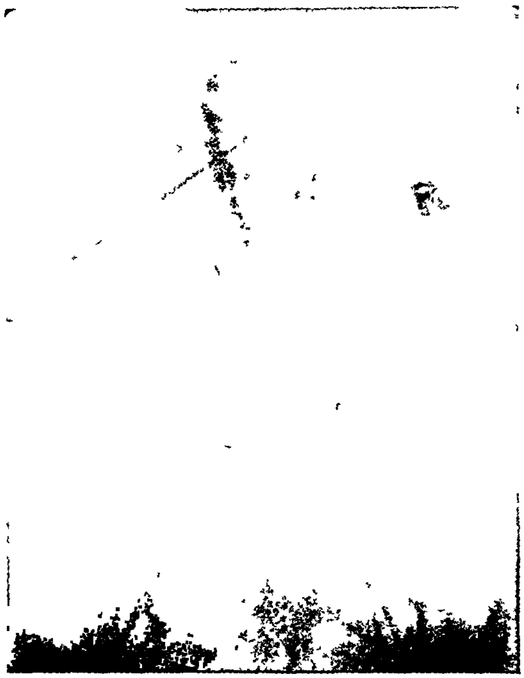

FIG 1. Aortogram showing occlusion of abdominal aorta Note silver clips of previous bilateral sympathectomy

was a sparcity of hairs of the legs, which were comparatively cold to the touch. She had global atrophy of both legs, more marked in the left. Her walk was a slow, cautious gait, and she was able to walk only a measured 40 feet before having to stop because of leg cramps. After a short rest, she was able to continue again. Because her right leg was less involved than her left, she was able to walk half a block by using crutches before developing hip pains and leg cramps.

Translumbar aortogram with 25 per cent diodrast revealed occlusion of the aorta below the renal vessels (fig. 1). An excellent nephrogram was also obtained. Injection of similar contrast material through the small, pulseless femoral arteries showed the vessels to be patent distally below the inguinal ligament.

On June 7, 1955, under general anesthesia, through a transverse abdominal incision below the umbilicus, a hard, calcified, pulseless, abdominal aorta and its bifurcation were exposed and resected from just below the superior mesenteric artery to the bifurcation of both common iliacs into the external iliac and the hypogastric arteries. The shrunken, resected arteriosclerotic vessels were completely occluded by the calcified thrombosed and gelatinous-like contents within the lumen, which extended superiorly and inferiorly on both sides beyond the limits of the resection. No free bleeding was obtained from the open end of the aorta superiorly or from either open vessel inferiorly until the plugs within these lumens were removed by thrombo-endarterectomies. Following this there appeared to be no obstruction from the aorta above or from the right hypogastric and external iliac arteries, but blood welled up less freely from the left external iliac and hypogastric vessels. Further resection was limited because only one lypholized homograft of the aorta and its bifurcation was available, which was sutured in place. It was felt that blood flowed freely from the aorta through the graft to the right vessels, but that the flow to the left vessels was much more limited

Her postoperative course was uncomplicated *She had no further urinary incontinence* Her hip pains and numbness and coldness of her lower extremities disappeared All pulses of the right leg were strong and definite, those of the left leg were only very faintly palpable Five months after operation the patient reported the following intermittent claudication, which previously even awoke her from sleep, is only occasionally present after exercise and much more mild than preoperatively, she no longer has the preoperative fatigue of her right leg, and that of her left is much more mild, the numbness and coldness of her legs are no longer present, pains and cramps in her back, hips, pelvis and legs, extending to her calves, have disappeared, except for milder pains of her left hip and leg, she has noted growth of hair on her legs, libido is definitely increased (preoperatively she had practically abstained from sexual relations for approximately two years), she is now able to walk 1½ to 3 blocks (as compared to 40 feet preoperatively) before left hip and leg cramps develop, but these are less severe than preoperatively and require a shorter rest period for relief, and, although the excellent condition of her right leg now permits her to walk an indefinite distance with crutches, she no longer uses crutches, even when going shopping Blood pressure in her right leg is now 150/100 while that in her left is heard faintly at 110 mm Hg She very occasionally may wet her step-ins slightly, but this is unusual and she now has excellent urinary control

COMMENT

This case report is presented primarily because the patient's severe urinary incontinence (which over a period of years had failed to respond to all other treatments, including repair of a cystocele and plication of the urethra) was immediately, dramatically and practically completely cured following resection of the occluded portion of the abdominal aorta and its bifurcation and replacement with a lypholized homograft This was undoubtedly due to the increased blood supply to the pelvic region

Inability of the male to keep a stable erection and impotency—symptoms commonly seen in the more numerous male patients with Leriche syndrome—and the improvement in these symptoms following aortic grafting may be explained on the same basis It is noted that our patient's libido was improved by operation

It is accepted generally that a thrombosed vessel is no longer a part of the arterial system, and with occlusion becomes a carrier of vaso constriction impulses, and also originates reflex arteriospasm These effects extend not only to the vessels of the extremities, but to the vessels of the pelvis and to all organs supplied by these vessels

Since the availability of aortic grafts, re evaluation of numerous cases previously diagnosed as Buerger's disease have shown these cases to actually be Leriche syndromes It is suggested that cases of urinary incontinence, a symptom not previously attributed to Leriche syndrome, may also in numerous cases be due to this pathological entity and may respond to surgical resection of the occluded blood vessels and replacement with grafts

SUMMARY

A case of Leriche syndrome with urinary incontinence in the female successfully treated by excision of the occluded vessels and replacement with a homograft is reported.

Urinary incontinence, as demonstrated by this case, is a symptom not previously attributed to the Leriche syndrome.

It is suggested that other cases of urinary incontinence, especially in the female, may be due to this etiological entity which should be considered in the differential diagnosis of these cases.

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THE JOURNAL OF UROLOGY
Vol 75 No 6 June 1956
Printed in U.S.A.

SECONDARY MALIGNANT TUMORS OF THE URINARY BLADDER METASTATIC FROM PRIMARY FOCI IN DISTANT ORGANS

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Bladder tumors may be broadly classified as primary or secondary tumors[1] Secondary tumors may be further subdivided into 4 groups as follows

1) Those that reach the bladder by direct extension from a primary focus in an adjacent organ, such as the cervix uteri, prostate gland, rectum, or sigmoid colon

2) Those that reach the bladder by reimplantation of exfoliated cells from a transitional cell epithelioma of the ureter or renal pelvis, or develop simultaneously in the bladder and renal pelvis or ureter as a result of stimulation by an unknown carcinogen of multicentric pre malignant foci present in the urothelial tract

3) Those that involve the bladder secondary to lymphoma or leukemia

4) Those that reach the bladder by lymphogenous or hematogenous metastasis from a primary focus in a distant organ, such as the stomach or breast

This communication is concerned with the type 4 tumor, an example of which is presented in the following case report

CASE REPORT

A 71-year-old single woman was first seen in March 1945, complaining of a lump in the left breast of 18 months' duration

Physical examination revealed a hard mass, measuring 4 cm in diameter in the upper lateral quadrant of the left breast with skin retraction visible over the mass There was no palpable axillary or supraclavicular lymphadenopathy The liver was not palpably enlarged

The urinalysis, nonprotein nitrogen determination and blood counts were within normal limits Metastatic x-ray series showed no demonstrable bone metastases

A left radical mastectomy was performed Pathologic report of the surgical specimen was adenocarcinoma of the breast, grade 3 to 4, with local invasion of the lymphatics but no demonstrable metastases in the axillary nodes (fig 1, *A*)

The convalescence was smooth and the patient remained well until May 1952, seven years later, when she was re admitted for evaluation of a small ulcerative lesion measuring 0 7 cm in diameter in the left anterior chest wall, 4 cm medial to the mastectomy scar

Bone x-rays now showed metastases in the right ilium and skull

Surgical excision of this lesion with the underlying fifth rib was carried out On microscopic examination, this was shown to be metastatic carcinoma to the skin and fifth rib (fig 1, *B*)

Estrogen treatment was now begun, the patient receiving 5 mg stilbestrol daily

Accepted for publication January 26, 1956

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[1] Melicow, M M J Urol, 74: 498, 1955

stated that "the eye, middle ear, pineal, and nasopharynx were practically the only tissues to be spared."

In an autopsy study of 67 cases of gastric carcinoma, Warren[29] found only 1 case that showed metastasis to the urinary bladder.

In explaining the mechanism of such widespread breast tumor metastasis, Warren and Witham state that the evidence is fairly strong that minute viable tumor emboli may pass through the pulmonary circulation without establishment of lung metastasis. Usually metastases occur by emboli into the lymphatics. When dissemination occurs by the bloodstream, the metastases in the lungs are usually the source of tumor emboli. Presumably, the same mechanism may be postulated for gastric carcinoma and malignant melanoma as well.

SUMMARY

A case is reported of a female patient with primary adenocarcinoma of the breast which subsequently metastasized to the urinary bladder and required segmental resection for control of gross hematuria. It is probable that minute viable tumor emboli passed through the pulmonary circulation without establishing lung metastases and thus set up metastasis in the bladder by hematogenous transport.

In one large series, metastatic tumors to the bladder from distant primary foci represented 1.54 per cent of all bladder tumors reported.

A review of the literature revealed a total of 80 cases, the majority of which were autopsy reports of patients who presented no clinical urological diagnostic or therapeutic problems. Among the minority, the chief problem was control of hematuria, which was effected by segmental bladder resection, transurethral resection, or suprapubic cystostomy.

The presence or absence of hematuria and symptoms of bladder irritability would seem to depend on the ability of the tumor emboli in the bladder wall to grow rapidly, penetrate the bladder epithelium, and protrude into the lumen of the bladder before death occurs from the patient's primary malignancy.

The commonest primary tumors found to have given rise to bladder metastases in this series of 80 cases were, in order of frequency: 1) gastric carcinoma, 2) malignant melanoma, 3) breast carcinoma, and 4) carcinoma of the lung.

The authors wish to thank Dr. Harry C. East for his help in translating some of the foreign periodicals.

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The Journal of Urology
Vol. 75, No. 6, June 1956
Printed in U.S.A.

UNDESCENDED TESTES: REPORT OF 153 CASES WITH EVALUATION OF CLINICAL FINDINGS, TREATMENT, AND RESULTS ON FOLLOWUP UP TO THIRTY-THREE YEARS

JOHN R. HAND

In this series orchiopexy was deferred until puberty unless complications demanded earlier intervention. Such a course resulted in placement of some testes before puberty. It allowed others to descend spontaneously. It encouraged trial of chorionic gonadotrophin to aid descent of still others, with completion of descent in a small number.

Evaluation of results was aimed at: 1) the cosmetic status as evidenced by position, size and consistency of the testes after they had reached the scrotum by delayed descent or orchiopexy, 2) the physiologic status of these testes.

The study calls attention to the significant number of testes that were retained after puberty, and emphasizes the damage that ensued. It also points up the variation in the behavior of individual testes, even in the same patient.

DESCRIPTION OF MATERIAL

The series includes 153 consecutive patients seen by the physicians in The Portland Clinic from January 1, 1922 to April 1, 1955. Fifty-one had bilateral and 102 had unilateral retention, making a total of 204 testes involved.

Three patients were not traced. In discussing some clinical features all 153 patients are included. In other instances only the 150 traced are considered. The latter had involvement of 199 testes—49 patients having bilateral and 101 unilateral retention.

To evaluate clinical factors and compare results in different categories, the patients were grouped according to the fate of one or both testes (table 1). Management of 20 testes was carried out elsewhere.

CLINICAL FINDINGS

Age. Table 2 shows the 3 age groups in which the testes of the respective patients descended to the scrotum or were managed by some operative procedure. When both testes did not reach the scrotum at the same time, the age the first did is shown. Patients under observation and those who have not had treatment as advised are listed according to their ages on admission. The youngest patient was 2, the oldest 73.

There were 8 adults in the bilateral group and 52 in the unilateral group. This wide difference emphasizes the lack of concern the patient with unilateral retention has regarding his abnormality, particularly when it has not impaired his potency or fertility and has not given rise to psychic trauma. The majority of these adults required orchiectomy because treatment had been neglected.

Side of involvement and position of testes. Of the 204 testes, 115 were on the right and 89 on the left side.

Abridgement of paper read at annual meeting American Association of Genito-Urinary Surgeons, Pebble Beach, Calif., May 19-21, 1955.

For full length paper, see Trans. Am. Assoc. Genito-Urin. Surg., 47: 9-30, 1955.

TABLE 1. *Fate of 204 undescended testes in 153 patients*

Fate of Testes Here and Elsewhere	Bilateral Retention		Unilateral Retention
	No pts.	No. testes	No. pts. and testes
Delayed descent	13	26	8
1 side delayed descent, 1 side other fate*	10	20	—
1 side orchiopexy, 1 side other operation†	4	8	—
Orchiopexy‡	18	36	40
Primary orchiectomy	—	—	30
Explored, not found	1	2	3
Epididymal remnants removed	—	—	4
Testes replaced in abdomen	1	2	—
Under observation	2	4	1
Treatment not followed as advised	—	—	15
Not traced	2	4	1
Total	51	102	102

* Orchiopexy, 6 testes; orchiectomy, 1; exploration, 1; epididymal remnant removed, 1, under observation, 1.

† Primary orchiectomy, 3 testes; epididymal remnant removed, 1.

‡ Secondary orchiectomy, 4 testes—1 patient with bilateral and 3 with unilateral retention.

TABLE 2. *Ages of 153 patients with undescended testes*

Age Treatment Was Done or Advised	Total Patients		Bilateral Retention		Unilateral Retention	
	No.	%	No pts	%	No pts.	%
Prepuberal 1 through 9	30	19.61	19	37.25	11	10.78
Puberal 10 through 17	63	41.18	24	47.06	39	38 24
Adult 18 and over	60	39.21	8	15.6	52	50.98
Total	153		51		102	

The position of 8 testes could not be ascertained in patients operated on elsewhere prior to admission. Fifty-two testes could not be palpated on examination here. Of these, 3 were in patients not traced and 6 in patients not treated. Eleven subsequently descended spontaneously, either from the abdomen or the canal. Operation disclosed 11 instances of agenesis; it also showed arrest of 9 testes in the abdomen and 11 in the canal. Autopsy revealed 1 ectopic testis.

The remaining 144 testes were palpated on clinical examination. Adding these to the 21 testes located at operation and autopsy gives a total of 165 testes with known levels of arrest. These were: abdomen, 9; canal, 73; external ring, 61; ectopic position, 22. Of the 22 testes, 2 proved to be in the femoral region, 2 in the pubopenile area and 18 in the superficial inguinal pouch described by Browne. This pouch lies between Scarpa's fascia and the external oblique and includes the space superior, lateral and inferior to the external ring.

Size of testes. The size of the testes at the initial examination was recorded in 103 instances. Fourteen were normal, 86 small and 3 large because of tumor (a fourth tumor was intra-abdominal).

Retractile testes As used here, "retractile" refers to testes that retract out of the scrotum after temporary residence (as revealed by the history and repeated observation) or when the fingers manipulating them toward the scrotum are withdrawn

Of the 153 patients, 13 had 19 retractile testes Thirteen subsequently descended spontaneously, 1 not coming down until the patient was 21, despite its retractability Six were put in position by orchiopexy Of these, 4 were associated with clinical hernias and 1 was arrested in the superficial inguinal pouch The sixth, brought down by orchiopexy elsewhere, had not been associated with a hernia on previous examination here

Four of the 19 testes had had temporary scrotal residence The size on admission was recorded for 9 of these testes, 6 being small and 3 normal

Hereditary tendency Members of the families of 14 patients had undescended testes—the uncle of 1, the brothers of 5, the fathers of 2 and 9 sons of 6 patients The mother of still another patient had agenesis of 1 ovary

Thus, a tendency to abnormality of the testes or ovary was exhibited by members of the families of 15 patients, or 9 8 per cent Since 11 had bilateral and 4 unilateral retention, the ratio of an hereditary tendency is 1 to 5 in the bilateral group of 51 patients and 1 to 25 in the unilateral group of 102 patients

Associated abnormalities Thirty-nine patients had additional abnormalities, as follows mental retardation, 8 (1 is in an institution), schizophrenia, 2, involutional melancholia, 1, obesity, 7, eunuchoid characteristics, 8 (2 puberal boys, 6 adults), gynecomastia, 6 (bilateral in 1), deafness, 2, congenital dislocation of the hips, 1, perineal hypospadias, 2 One of the last 2 had an abdominal exploration prior to admission and no female organs were found

TREATMENT

No treatment In 14 patients 22 testes descended spontaneously in that they were not subjected to hormone stimulation or operation But in 4 of these patients the retained mate required operation

Hormone therapy Injections of chorionic gonadotrophin were given to 47 patients with involvement of 69 testes The amounts ranged from 1,625 to 50,000 international units Only 4 patients received 36,000 units or more

Descent was attributed to the hormone if the testes came down within a month after its administration On this basis, 16 testes responded to treatment Four were the patients who had received the large amounts of hormone

The youngest patient to receive chorionic gonadotrophin was 7 years old The youngest to show response was 8 years old

Not responding to hormone stimulation, but subsequently descending spontaneously at puberty were 6 testes of 4 patients The failure of these to respond was probably due to an insufficient amount of hormone Yet, in 1 patient the mate had responded to the hormone stimulation 2 years previously

Recapitulation of testes descending without operation (spontaneous descent) From the foregoing, and as noted by others,* it is evident that a significant number of retained testes do not require orchiopexy

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* Bishop Deming, Johnson McCutcheon, Mimpriss, Rea, Smith (1951), Thompson Bevan, Heckel, McCarty and Thompson See list of references for place of publication

TABLE 3. *Age at which 44 testes in 31 patients descended spontaneously—with and without hormone stimulation*

Explanation of Descent	No. Pts	No Testes	Age Testes Descended										
			Prepuberal			Puberal						Adult	
			7	8	9	10	11	12	13	14	15	18	21
Bilateral retention:													
Both same age	7	14	—	—	6	2	—	6	—	—	—	—	—
Each different age	6	12	1	—	1	2	—	4	2	—	1	1	—
One side only	10	10*	—	1	3	—	1	2	—	1	1	—	1
Unilateral retention	8	8	1	—	—	3	1	3	—	—	—	—	—
Total	31	44	2	1	10	7	2	15	2	1	2	1	1
			13 (29.55%)			29 (65.91%)						2 (4.55%)	

* The fates of the opposite 10 testes were: orchiopexy, 6 at ages 9 to 12; orchiectomy, 2 at ages 23 and 49; agenesis on exploration at age 14, 1; still under observation at age 9, 1.

While testes that descend spontaneously are generally not considered to be in the same category as testes that must be brought down, they have been included here for 2 reasons. First, they demonstrate the wide age range of delayed descent. Second, their long residence outside the scrotum and their subsequent corrected position without operative trauma make evaluation of their status after reaching the scrotum a good yardstick for comparison with the status of testes placed in position by orchiopexy.

There was, then, descent without operation in a total of 44 testes—in 31 patients, of whom 23 had bilateral and 8 unilateral retention. This represents 22.1 per cent of 199 testes in 49 patients with bilateral and 101 with unilateral retention who were traced. Hence, the ratio of descent was 1 to 2 among patients with bilateral retention and 1 to 9 among those with unilateral retention.

Although 23 of the 31 patients had bilateral retention, only 13 had bilateral descent. In 7 patients both testes came down simultaneously; in 6 there was a lapse of from 2 to 6 years between descent of the first and second testis. In 4 of the 6 patients the right testis lagged behind the left.

The relationship of age to descent and the side involved is shown in table 3. At the initial examination, 8 of the 44 testes were palpable in the canal and 22 at the external ring. Eleven could not be palpated and may have been either in the abdomen or in the canal. Three testes had descended prior to admission, from positions not determined. None was palpable in an ectopic position. None was associated with a clinical hernia.

Operative correction. Shown in table 4 are the various operations carried out here and elsewhere on 138 clinically undescended testes. The one-stage orchiopexies were modifications of the procedures described by Bevan and by Cabot and Nesbit. The two-stage orchiopexies were those developed by Torek and by Keetley.

Of the 86 orchiopexies, 67 were done by puberty. Four testes were later

TABLE 4 *Operations for 138 clinically undescended testes*

Procedure	Total Ops	Side Involved		Age at Operation			Ops Else
		Bil	Unil	Prepub	Puberal	Adult	
1 stage orchiopexy	59	32	27	15	33	11	8
2 stage orchiopexy	27	15	12	5	14	8	1
Secondary orchiectomy	4	1	3	—	—	4	1
Primary orchiectomy	35	5	30	—	3	32	7
Explored, not found	6	3	3	—	6	—	1
Remnants of epididymis or vas removed	5	1	4	—	—	5	—
Both testes put in abdomen, rings closed	2	2	—	2	—	—	2
Total	138	59	79	22	56	60	20

removed. Thirty two of the primary orchiectomies were done on patients with unilateral retention seen after puberty.

Complication of hernia. It is important to remember that while the potentiality of hernia is always present in the undescended testis, the hernia may not become of clinical significance.

In this series there were 89 concomitant hernias, 85 of which were repaired. Of those repaired, 18 were in prepuberal boys, 34 in puberal boys and 33 in adults.

Sixty seven hernias were repaired here, of which 42 had been diagnosed clinically and 25 detected at operation for correction of the retention. One testis retracted after one stage orchiopexy and herniorrhaphy at age 5.

Eighteen hernias were repaired elsewhere. When the patients were subsequently seen here, 7 testes were palpated at the external rings. Five had retracted following one stage orchiopexies and herniorrhaphies at ages 2, 5, 6, 11 and 49; 2 were not put in position when the concurrent hernias were repaired at ages 30 and 43. Two hernias in 2 other patients recurred. In still another patient both testes were replaced in the abdomen at age 8 and the external ring on each side was closed tight when bilateral hernias were repaired.

While none of the 44 testes that descended spontaneously had a concomitant hernia, hernias developed after the descent of 4. The intervals between descent and detection of the hernias were 6 months, 6 months, 2 years and 10 years.

Complication of torsion. Torsion developed in 3 patients. One had a single attack at age 12, 1 had an attack at age 30, the third had recurring episodes past puberty. The involved testis of the first patient, brought down by orchiopexy, was subsequently atrophied; the testes of the 2 adults had to be removed.

Complication of tumor. Seminoma was a third complication, being present in 4 testes. One was arrested in the right side of the abdomen, 1 in the right canal, 1 in the right and 1 in the left superficial inguinal pouch.

The ages of the patients at orchiectomy were 26, 36, 37 and 39. Three had normally descended mates, 1 of which was atrophied; the fourth had an atrophied canalicular mate.

In The Portland Clinic there were 26 additional patients who had cancer in

TABLE 5. *Relationship of position to fate of testes*

Known Level of Arrest	Number of Testes					Fate of Testes								
	Total	Side		Elim-inated*	Included	Orchiopexy			Orchiectomy			Delayed descent		
		Bil	Unil			Bil	Unil.	%	Bil.	Unil.	%	Bil.	Unil.	%
Abdomen	9	3	6	—	9	4	—	44.44	1	4	55.56	—	—	—
Canal	73	31	42	5	68	22	18	58.81†	3	17	29.41	6	2	11.76
External ring	61	38	23	8	53	18	8	49.06	—	5	9.43	17	5	41.51
Ectopic	22	8	14	4	18	4	9	72.23	1	4	27.78	—	—	—
Total	165	80	85	17	148	48	35	56.08	5	30	23.65	23	7	20.27

* Includes 6 testes (4 patients) expectant treatment; 9 in patients who have not had treatment as advised; 2 in patients not traced.

† 3 testes, 1 in patient with bilateral and 2 in patients with unilateral retention, subsequently removed.

28 scrotal testes. On the basis of 32 malignant testes, the percentage of cancer in undescended testes in this clinic is 12.5 per cent; on the basis of 199 clinically retained testes in 150 patients traced, the percentage is 2.01. When the 44 testes that descended spontaneously are deducted, the percentage is slightly higher, being 2.76.

Malignancy was not observed in testes brought down by orchiopexy nor in those descending spontaneously.* Gilbert and Hamilton stated that orchiopexy does not prevent latent malignancy. They observed cancer in 77 testes after orchiopexy. Rusche noted malignancy in 4 testes subjected to such operations.

Associated defects. Gross developmental anomalies were detected in 17 testes of 15 patients. While 4 patients had bilateral retention, only 2 had bilateral defects. Eleven defects represent agenesis; 2 excessively short cords; 4 hypoplasia of the testes. In 1 patient the hypoplastic tissue removed from the external ring contained ovarian as well as testicular elements.

Relationship of position to fate of testes. Table 5 shows the relationship of the known levels of arrest to the fate of the testes. Factors held responsible for unilateral retention were also noted in bilateral retention.

For example, among the 85 unilaterally retained testes, 7 descended spontaneously. Eliminating these 7 and 11 with gross defects, leaves 67 mechanically obstructed. Among the 80 testes in the bilateral group, 23 descended spontaneously. When these 23 and 6 with gross defects are eliminated, there remain 51 mechanically obstructed.

The largest number of bilaterally retained testes were arrested at the external rings, 38 of 61. The unilaterally retained testes were most often arrested in the canals, 42 of 73.

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* After this paper was submitted for publication, 1 patient had orchiectomy (February 10, 1956) for pain in a testis brought to the scrotum from the canal 7 years previously, when he was 39 years old. Histologic study showed seminoma. At age 39 the mate had been removed from the superficial inguinal pouch because of seminoma.

EVALUATION OF MICROSECTIONS

Sections were available for review from 36 testes in the series For comparison, sections were also obtained from 5 normally descended mates The findings are grouped according to the time the tissue was obtained

1 *Biopsy at orchiopexy* Included here are sections of 6 undescended testes from patients 13, 14, 17, 17 and 25 years old In each the tubules were smaller than normal and the tunica propria as well as the basement membrane was thickened The section from the testis of the boy aged 14 showed Sertoli cells only (fig 1, *B*) In sections from the other 5 testes, tubules with Sertoli cells only were present alongside tubules containing Sertoli cells and spermatogonia In 3 testes maturation had progressed to the primary spermatocyte stage—1 was the testis of a boy 17 and 2 were the testes of the man aged 25 The latter was the oldest patient in the series with some preservation of germinal elements In the section from the testis of the 13-year-old boy an occasional prepuberal tubule persisted Leydig cells were preserved in the sections of all 6 testes

2 *Biopsy after scrotal residence* In this group there are sections of 5 testes put in position by two stage orchiopexies 4 to 10 years earlier The sections were obtained at ages 17, 18, 22, 23, and 24 Spermatogenesis was complete in 4 and arrested at the spermatid stage in 1 Despite the scrotal residence, the spermatogenesis was focal, being present in only one sixth of the tubules in each section (fig 2) Leydig cells were preserved in all

Since the orchiopexies in this group were all two stage procedures, it would seem that the degeneration resulted from injury to the blood supply during lengthening of the cord or from narrowing of the blood vessels as a result of vascular spasm or tension incident to securing the testes to the thighs However, for accurate assessment of the role orchiopexy plays in degeneration it would be necessary to compare sections of the testes at the time of operation with those at follow up

3 *Extirpated testes* Included here are 25 undescended testes Sections from testes of 2 boys aged 12 and 15 showed spermatogonia Section from the testis of a boy 17 showed Sertoli cells only In the sections of all 3 testes there were prepuberal tubules

The testes of 22 adults, 18 to 72, all showed degeneration of germinal elements In 5 the degeneration had progressed to destruction of Sertoli cells Leydig cells were noted in all but 2 sections Prepuberal tubules were present in 5 sections, indicating congenital defectiveness

4 *Normally descended mates* Sections were obtained from 5 normally descended mates Four showed no abnormalities The fifth, from a boy aged 13, contained prepuberal tubules and thick walls together with maturing tubules, as had been observed in his retained testis

POSTOPERATIVE TREATMENT

Four patients are being maintained on testosterone by intramuscular injection and buccal absorption The former is delatestryl (Squibb) in sesame oil It is

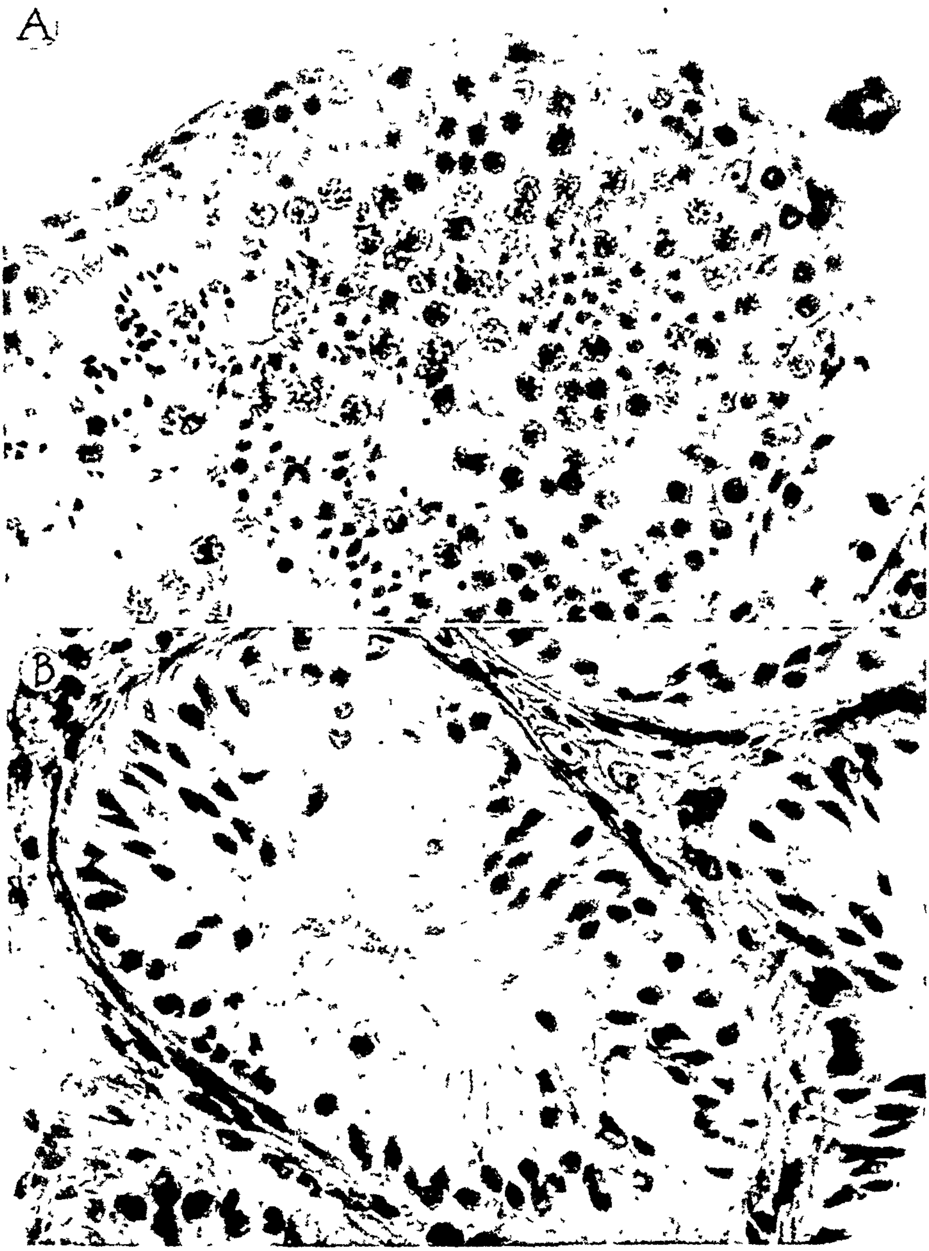

Fig. 1. Boy aged 14. *A*, normally descended testis showing spermatogenesis. *B*, mate brought down from external ring. Tubules contain Sertoli cells only.

injected deep in the gluteal muscle every 6 weeks in doses of 1 cc or 200 mg. The latter is oreton-M (Schering's methyl testosterone), in 10 mg. tablets taken 1 to 4 times a day as necessary.

Chorionic gonadotrophin was used successfully as an adjunct to orchiopexy in a puberal boy who had poorly developed genitalia. He subsequently married and fathered 2 children.

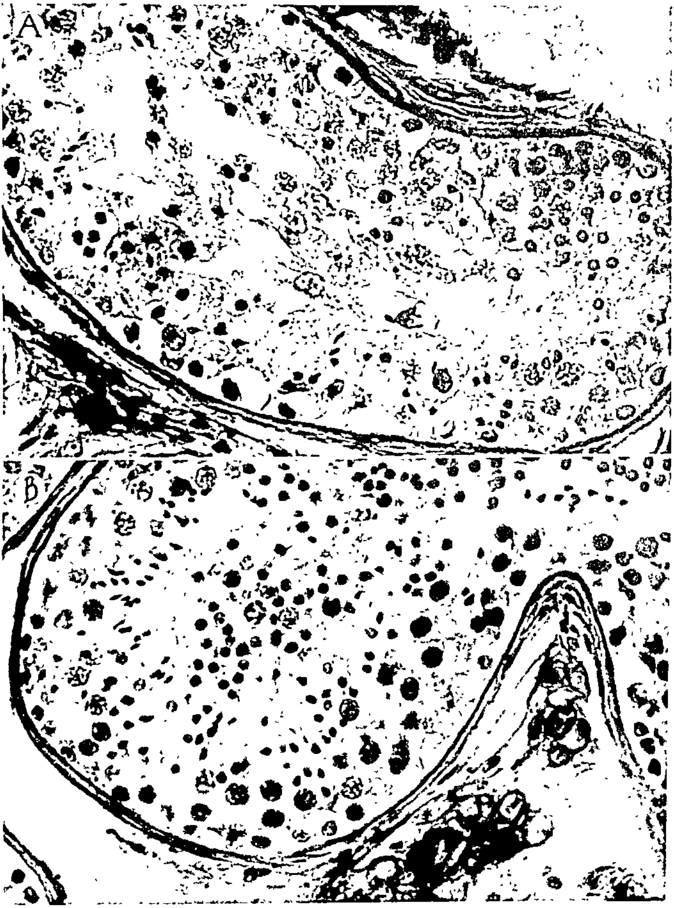

Fig. 2. Man aged 22. *A*, normally descended testis Spermatogenesis is present. *B*, mate brought down by Torek operation from canal at age 12. While spermatogenesis was present, it was noted in only one-sixth of the tubules studied.

FOLLOWUP

Of the 150 patients traced, 141 are alive; 9 are dead. The length of the followup was: 6 to 11 months, 19 patients; 1 to 9 years, 54; 10 to 19 years, 45; 20 to 29 years, 28; 30 to 33 years, 4. This represents the interval from the time one or both testes reached the scrotum or were removed, or from admission when treatment was incomplete, to the end of the followup on April 1, 1955 or death.

TABLE 6. *Cosmetic results on followup examination*

Status of Testes	Spontaneous Descent			Orchiopexy					
	44 Testes			1 Stage 59 Testes			2 Stage 27 Testes		
	Normal	%	Abn.	Normal	%	Abn	Normal	%	Abn.
Position	42	95.35	2	42	71.19	14	25	92.59	—
Size	40	90.7	4	30	50.85	26	11	40.74	14
Consistency	42	95.35	2	38	64.41	18	14	51.85	11
Not palpable because of atrophy or subsequent orchiectomy	—	—	—	—	—	3	—	—	2

TABLE. 7 *Summary of marital status on followup of patients traced*

Status of Patients	49 Patients with Bilateral Retention		101 Patients with Unilateral Retention	
	No pts.	%	No. pts.	%
Traced	49		101	
Married	24	48.98	61	60.39
with children	15	62.5	47	77.05
without children	9	37.5	14	24.19
Single adults	14	28.57	18	17.82
Adolescents	11	22.45	22	21.78

Seventy-five patients responded to a questionnaire, 66 came in for re-examination. The 4 patients who had seminomas have been alive 5, 6, 6½ and 15 years, respectively.

Cosmetic results. Table 6 shows the position was better after the two-stage orchiopexy, but the size and consistency of the testes were better after the one-stage procedure. The greatest number of good results in all three respects were among the testes that had descended spontaneously. Four were small after spontaneous descent—3 having come down at puberty, 1 at age 21.

The cremaster reflex, which one would expect to approach normal after spontaneous descent, has been absent or weakly positive in patients examined thus far. Absence of the cremaster reflex is expected after orchiopexy.

Fertility in married patients with bilateral retention. The marital status of the 49 patients with bilateral retention who were traced is presented in table 7.

Fifteen of the married men had children. The fate of the testes of these men is listed in table 8. In all but 1 man, one or both testes were in the scrotum by puberty.

The highest incidence of fertility was among the 13 men whose testes had both descended spontaneously before or during puberty. Six were married, and all were fertile, having fathered from 1 to 4 children.

Spontaneous descent on 1 side at puberty was responsible for the fertility of 2 other men who had, respectively, 3 and 8 children. In 1 the mate was removed from the abdomen at age 23; in the other there was agenesis on the opposite side. Thus, spontaneous descent was responsible for the fertility of 8 men.

Of the men who had bilateral orchiopexies, 9 are married. Four have had

TABLE 8 *Evaluation of fertility of 15 married men with bilateral undescended testes*

Fate of Testis	Total Pts	No Married	No with Child	%	Age of Fertile Men at Operation or Descent of Testes		
					Prepub	Puberal	Adult
Bil spontaneous descent	13	6	6	100 00	2	4	—
Bil orchiopexy	18	9	4	44 44	—	4	—
1 side spont descent, 1 side orchiopexy	6	4	2*	50 00	2	—	—
1 side spont descent, 1 side orchiectomy	2	1	1	100 00	—	1	—
1 side spont descent, 1 side agenesis	1	1	1	100 00	—	1	—
1 side orchiopexy, 1 side orchiectomy	4	2	1†	50 00	—	—	1
Both put in abdomen, rings closed	1	1	—	—			
Total	45	24	15	62 50	4	10	1

* *One patient had orchiopexy at 8 and descent at 21 Orchiopexy likely contributed to fertility*

† Both operations done at age 53 Son born when patient 41 Orchiopexy cannot be credited with producing fertile testis

children—1, 2, 2 and 3, respectively Each of the 4 had had a one stage orchiopexy at puberty These plus 1 man who was fertile after unilateral one stage orchiopexy at age 8 and spontaneous descent of an atrophied mate at age 21, make 5 men whose fertility can be ascribed to one stage orchiopexy

In MacCollum's series of 11 patients having bilateral orchiopexies, 6 had children Coley reported paternity in a man who had had bilateral orchiopexies—at age 30 on 1 side and age 45 on the other Bishop reported paternity in 1 patient after spontaneous descent of 1 testis at age 16 and removal of the mate at age 20

Infertility in married patients with bilateral retention In table 9 an attempt is made to explain the possible reasons for the infertility of 9 married men with bilateral retention Although the testes of 3 had reached the scrotum by puberty, their function was impaired

Probability of fertility in single adults with bilateral retention Of the 14 single adults, 7 must be eliminated from evaluation of potential fertility because of gonadal anomalies, 3 patients (bilateral in 2, associated with an atrophied mate in 1), confinement in a mental institution, 1, priesthood, 1, death, 2

Another patient, now 29 years old, has grand mal epilepsy and is mentally retarded He will probably not marry In still another patient prognosis must be guarded Both testes were brought down from the external rings by two stage orchiopexies at age 15 Recheck at age 23 showed both testes to be soft Biopsies at this time disclosed focal spermatogenesis, tubular degeneration and prepuberal tubules

Fertility is probable in the remaining 5 single adults Four, now 18, 19, 29 and 34 years old, had had bilateral spontaneous descent, all testes reaching the scrotum by age 12 The fifth man, now 21, had had spontaneous descent on one side at age 9 and two stage orchiopexy on the opposite side at age 13 On recent

TABLE 9. *Evaluation of infertility in 9 married men with bilateral undescended testes*

Case	Fate of Testes	Age at Operation or Descent of Testes			Followup	
		Prepub.	Puberal	Adult	Present age	Comment
1	Both put in abdomen, rings closed	8 & 8	—	—	49	Eunuchoid appearance
2	1 side spontaneous descent, 1 side orchiopexy 1 stage	—	12 & 13	—	33	Few spermatozoa in ejaculate; no scrotal development; obesity
3	1 side spontaneous descent, 1 side orchiopexy 1 stage	—	12 & 25	—	33	Nonmotile spermatozoa in ejaculate
4	Bilateral orchiopexy 1 stage	—	11 & 11	—	27	Gonadotrophic surveys high, indicating testicular failure
5	Bilateral orchiopexy 1 stage	—	—	21 & 21	33	Hypogonadotrophic hypogonadism
6	Bilateral orchiopexy 1 stage	—	—	25 & 25	25	Biopsy—primary spermatocytes. Few nonmotile spermatozoa in subsequent ejaculate
7	Bilateral orchiopexy 2 stage	—	—	18 & 18	24	Biopsy—focal spermatogenesis. Aspermia, indicating blocked tubular system
8	Bilateral orchiopexy 2 stage	—	—	25 & 25	29	Aspermia
9	1 side orchiopexy 2 stage, 1 side orchiectomy	—	—	39 & 39	45	Seminoma; hypogonadism, hypothyroidism; maintained on testosterone

examination, the testes of all 5 men were of normal size and consistency and at the bottom of the scrotum.

Probability of fertility in adolescents with bilateral retention. Of the 11 adolescents, 2 now aged 11 and 12 are being treated for perineal hypospadias.

Fertility is probable in the remaining 9 boys. One or both of their testes reached the scrotum by puberty—8 descending spontaneously, 9 placed by orchiopexy (1-stage, 4; 2-stage, 5). One testis is still under observation although its mate came down spontaneously.

Recapitulation of fertility and infertility in patients with bilateral retention. Of the 49 patients, fertility was established by paternity in 15; is possible in 16; is not likely in 18, as explained.

Fertility and infertility in patients with unilateral retention. Table 7 gives the marital status of the 101 patients with unilateral retention who were traced.

Of the 61 married men, 47 or 77.05 per cent have had children. Table 10 shows the incidence of fertility according to the fate of the retained testis. The

TABLE 10 *Evaluation of fertility of 47 married patients with unilateral undescended testes*

Fate of Testes	Total Pts	No Married	No with Child	%	Age at Operation Descent or Admission			Chief Complaints on Admission			
					Prepub	Puberal	Adult	*Retention*	*Hernia*	Pain orchitis tumor	Other conditions
Delayed descent	8	3	2	66.67	—	2	—	2	—	—	—
Orchiopexy	35	12	11	91.67	2	6	3*	4	7	—	—
Secondary orchiectomy	3	3	2	66.67	1†	—	1†	—	2	—	—
Primary orchiectomy	30	23	16	69.56	—	1	15	—	11	2	3
Exploration or removal, epididymal remnants	7	5	4	80.00	—	1	3	1	—	1	2
No treatment	15	15	12	80.00	—	1	11	1	4	—	7
Total	98	61	47	77.65	3	11	33	8	24	3	12

* Patients had had children prior to admission

† Age at primary orchiopexy

table shows, further, that only 8 of the 47 fertile men had come for treatment of their undescended testes, and these 8 were seen before or during puberty. The others had come in because of hernia, pain, a mass, or complaints unrelated to the genitalia.

Fourteen of the married men had not had children, despite the fact that each had one normally descended testis.

Probability of fertility in single adults and adolescents with unilateral retention. Of the 18 single adults, 3 are priests. Among the other 15 patients, 7 had orchiopexies at a favorable age; these testes may contribute to fertility. In the remaining 8 patients fertility will have to depend on the normally descended testes.

Of the 22 adolescents with unilateral retention, 1 had agenesis and 1 is still under treatment. The testes of the other 20 patients reached the scrotum by age 12, and should contribute to fertility.

Recapitulation of fertility and infertility in patients with unilateral retention. Of the 101 patients, the retained testis presumably contributed to the fertility of 47 who fathered children; it may contribute to fertility of 29; it will not contribute to fertility of 25 because of congenital defects and prolonged retention.

DISCUSSION

The inguinal bursa merits attention because of its role in the course taken by the testis. According to Wells, it is formed by the 4 layers of the abdominal wall when they evaginate in preparation for the descent of the testis.

Normally, the external spermatic fascia, which covers the bursa, becomes closely attached to the dartos, and the bursa thus forms a pathway for the descent of the testis. In retention, the external spermatic fascia projects beyond the bursa, either as a broad band or an elongated cord of varying thickness

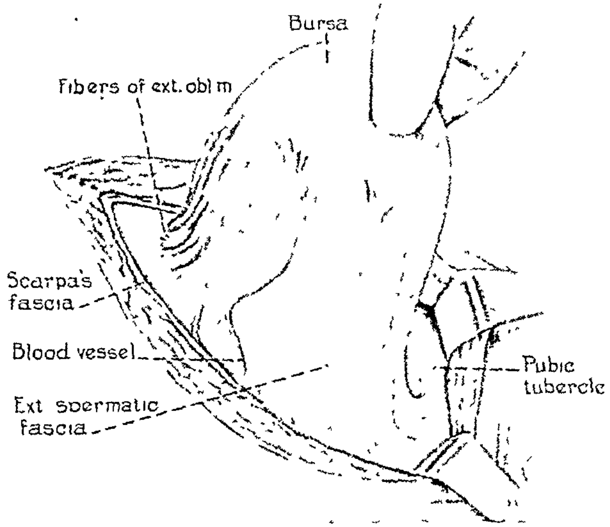

FIG. 3. Man aged 29. Portion of external spermatic fascia projecting beyond bursa is attached to pubic tubercle.

The direction that the projecting portion takes, together with the degree of bursal development and the level of its attachment determine whether the testis will continue to the scrotum in the normal line of descent or whether it will deviate from this course.

At operation for retention I have seen the bursa attached at a variety of abnormal levels (fig. 3). And on one occasion I saw the bursa with its outer layer of external spermatic fascia lying free within the superficial inguinal pouch.

Within the bursa the testis is mobile, the extent of its mobility being determined, largely, by the degree of bursal development. If the testis becomes more prominent as it is manipulated laterally, the bursa is arrested in the superficial inguinal pouch and, usually, attached to its lateral border. A testis that can be maneuvered into the canal through the external ring becomes less prominent, whether the bursa is directed normally or abnormally. The palpability of a testis in the canal depends on its size and the thickness of the abdominal wall.

It is generally agreed that the thermoregulating properties of the scrotum are necessary for testicular development; that after the age of 4 or 5 testes show first retardation in growth, then degeneration in proportion to the time that they remain outside the scrotum; and that some testes are intrinsically defective. But there is no general agreement regarding the time to place the testes in the scrotum, particularly when there are no complications, such as a clinical hernia, torsion and arrest in an ectopic position, all of which demand surgical intervention.

Some surgeons advocate orchiopexy in early childhood because of the changes Cooper and others have observed on histologic study of retained testes. In their opinions the retardation in development resulting from the retained position overshadows the possibility of spontaneous descent by puberty.

Other surgeons defer orchiopexy until early puberty unless complications make operation necessary before this. While they do not minimize the accumulating histologic evidence of the damage caused by prolonged retention, most of them take advantage of the latitude permitted by the considerable number of testes that come down at puberty

That deferment of orchiopexy until early puberty is justified is borne out by observations in this series As shown, not only the cosmetic results but also the percentage of proved fertility was better among patients who had had bilateral spontaneous descent than among those subjected to bilateral orchiopexy None of the 14 testes that had descended spontaneously came down before age 8 If they had been placed in position at age 4 or 5, all would have been subjected to needless operation and the possible irreparable damage from the trauma incident to this management Furthermore, retractability was not an infallible indication of ultimate descent since orchiopexy was necessary for 6 of the 19 retractile testes

Most surgeons now favor use of chorionic gonadotrophin to see if the testes will come down It is of particular value in the prepuberal boy with bilateral retention But this also may not be an accurate test In the present series, 6 testes not responding to hormone stimulation at an early age later descended at puberty

Two points bear emphasis First, while chorionic gonadotrophin may be given at any age, its use must not be deferred beyond puberty Since all boys do not mature at the same age, the appearance of the first pubic hair is a more reliable criterion of beginning puberty than age

Second, when the hormone is used, the amount given must be adequate, that is, large enough to insure descent, barring complications, but not to induce unfavorable genital development I use 4,000 international units 3 times a week up to 40,000 units, as suggested by Rogers and by Heller With this amount repetition of the treatment has not been necessary in my patients in this series and in those subsequently cared for

If the testes do not descend after adequate hormone therapy, exploration is indicated But this, too, must not be delayed beyond puberty

When the cord is of sufficient length to bring the testes to the bottom of the scrotum, I believe, with others, that a one stage operation is preferable to a two-stage operation In this series, placement by two stage orchiopexy kept the testes in the bottom of the scrotum Paternity after this operation, done at a favorable age, could not be evaluated because the patients who would have qualified were not married at the time of the followup But histologic study of 5 testes placed in position by two stage orchiopexies showed spermatogenesis in only one sixth of the tubules in each section The chief disadvantage of the two stage operation is the possibility of excessive tension on the blood vessels of the cord

In anchoring the testis in the scrotum, care must be taken not to obstruct the proximal vas which courses through the peritoneum just below the testis I have found the following procedure satisfactory

Two catgut sutures are passed through first the dartos, then the visceral layer of the tunica vaginalis and the tunica albuginea of the testis (fig 4) A third suture of silk, for traction, is introduced through the bottom of the scrotum, as near as possible to the septum, carried through the visceral layer of the tunica

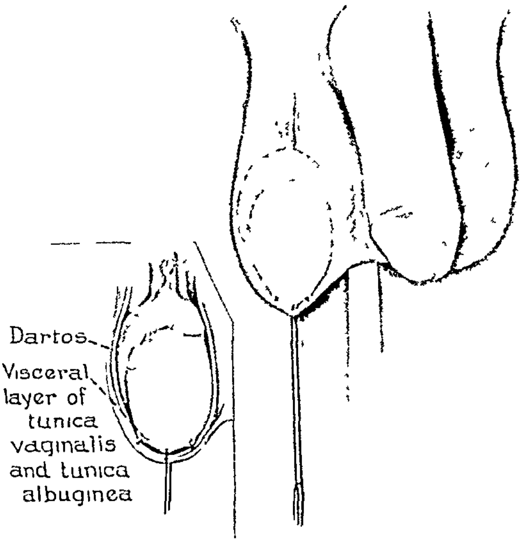

FIG. 4. Method of anchoring testis to dartos in one-stage orchiopexy. Note traction suture.

vaginalis and the tunica albuginea of the testis between the two previously placed catgut sutures, and brought out again through the bottom of the scrotum. The traction suture is then tied to a rubber band which is secured by adhesive tape to the thigh on the side of the orchiopexy. At the end of a week the traction suture is removed.

In repair of the operative site the Ferguson procedure of not transplanting the cord has distinct advantage. Brought out of the wound lateral to the pubic tubercle, the cord lies in a direct line to the scrotum. All the length that has been obtained is thus preserved. However, with this procedure it is necessary to make sure that the inguinal canal is left as strong as possible. When the structures of the inguinal canal appear to be deficient, it is better to transplant the cord and use fascia in the repair instead of catgut.

If bilateral undescended testes cannot be brought to the bottom of the scrotum, they should be placed in a high scrotal position or in a position outside the external ring rather than removed. Orchiectomy is advisable for the unilaterally retained testis that cannot be put in position in the bottom of the scrotum. At no time should a testis be put in the abdomen where detection of early malignancy would not be possible.

SUMMARY AND CONCLUSIONS

This series includes 199 testes in 49 patients with bilateral and 101 with unilateral retention, traced for periods up to 33 years.

Delayed descent occurred in 44 testes, 16 responding to hormone stimulation. Forty-two reached the scrotum at ages 8 to 15, 1 at age 18 and 1 at age 21.

Orchiopexies were possible for 86 testes—of which 59 were one stage and 27 two stage procedures Sixty seven were done by puberty Four testes were subsequently removed

Primary orchiectomy was done in 35 patients, 3 being puberal boys and 32 adults

In 67 instances there was either absence or partial to complete loss of testicular function because of gross congenital defects (17 instances), orchiectomy, or no treatment Most of these represent treatment delayed too long

Abnormalities associated with retention were obesity, eunuchoidism, gynecomastia, various neuropsychiatric disorders, hernia, torsion, malignancy

Microsections from 36 retained testes showed degeneration which progressed in proportion to the length of retention But the testes of a man aged 25 had preservation of germinal epithelium Prepuberal tubules persisted in the extirpated testes of 5 adults

Biopsy of 5 testes brought down by two stage orchiopexies 4 to 10 years previously showed persistent prepuberal tubules in 3 Spermatogenesis was complete in 4 and arrested in 1 However, the spermatogenesis was observed in only one sixth of the tubules in the section of each testis

The 4 patients with malignant testes have been alive, respectively, 5, 6, 6½ and 15 years The incidence of malignancy in this clinic is 12 5 per cent on the basis of cancer in 28 scrotal testes and 2 01 per cent on the basis of 199 clinically retained testes When the 44 testes descending spontaneously are eliminated, the percentage is 2 76

On followup, the position, size and consistency of the testes were better after spontaneous descent than after either the one or two stage orchiopexies Position was better after the two stage procedure, but size and consistency were better after the one stage procedure

Eight men fathered children after delayed spontaneous descent in contrast to 5 who fathered children after one stage orchiopexies done at puberty

From the observations in this series, it is concluded

The prepuberal testes should be given an opportunity to descend spontaneously, provided there are no complications such as clinical hernia, torsion or arrest in an ectopic position

Hormone stimulation can be used diagnostically before puberty, and is particularly valuable in bilateral retention But its use must not be delayed beyond puberty, as established by the appearance of the first pubic hair When used, the hormone must be given in adequate amount

If adequate hormone therapy does not effect descent, exploration is indicated, but must not be deferred beyond puberty

There is need of biopsies not only at the time of orchiopexy but also, for comparison, when the testes are released after fixation to the thighs in the two stage operation as well as after scrotal residence following both the one and two stage procedures There is also need for biopsies of testes that descend spontaneously after prolonged retention

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THE JOURNAL OF UROLOGY
Vol. 75, No. 6, June 1956
Printed in U.S.A.

FURTHER OBSERVATIONS ON THE REBOUND PHENOMENON IN THE TREATMENT OF CERTAIN TYPES OF SPERMATOGENIC DYSFUNCTION

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In 1951 a report was made on the increase in the number of spermatozoa in oligospermic men following the use of testosterone propionate.[1] In some of these patients a comparison of testicular biopsies taken prior to treatment with biopsies taken after treatment revealed a definite improvement in the spermatogenic activity. This observation, on testicular biopsies, confirmed a previous report by Heller and Nelson[2] who made an extensive histological study of testicular biopsies in apparently normal men who were given testosterone and found an improvement in testicular morphology and function.

During the past several years we have been interested in a more specific criterion for the selection of patients for treatment, and have included a review of a group of oligospermic men treated with testosterone propionate.

A total of 116 oligospermic patients who were physically normal and without evidence of endocrine disease have been treated. Testosterone propionate 50 mg. was given intramuscularly 3 times a week, or 200 mg. testosterone cyclopentylpropionate intramuscularly once a week.

Pretreatment testicular biopsies were secured in a majority of these patients.

A 50 million increase in total spermatozoa was arbitrarily selected as indicative of a "rebound phenomenon." Some patients had substantial increases but did not reach the required 50 million increase to qualify as a "rebound."

Insufficient evidence was available for classification of 32 of these patients. Seventy-three patients have been followed sufficiently to allow definite conclusions to be made. Of these, 28 patients (38 per cent) secured a spermatogenic rebound with total spermatozoa far exceeding their pretreatment level and in all instances an increase of at least 50 million over the pretreatment counts. Four of these patients receded to pretreatment levels in from five months to two years.

Forty-five patients did not secure a rebound. However, 13 of these had an increase of 13 to 46 million in the total spermatozoa counts, with an average increase of 32 million. In a review of the testicular biopsies of these patients, 11 had marked germinal cell atrophy, 3 had severe regional fibrosis, and 9 patients had no biopsies. None of these patients should have received treatment because of the inability of the germinal epithelium to respond or because of the unknown quantity in the absence of biopsy.

Read at annual meeting, North Central Section of American Urological Association, Chicago, Ill. September 29–October 1, 1955.

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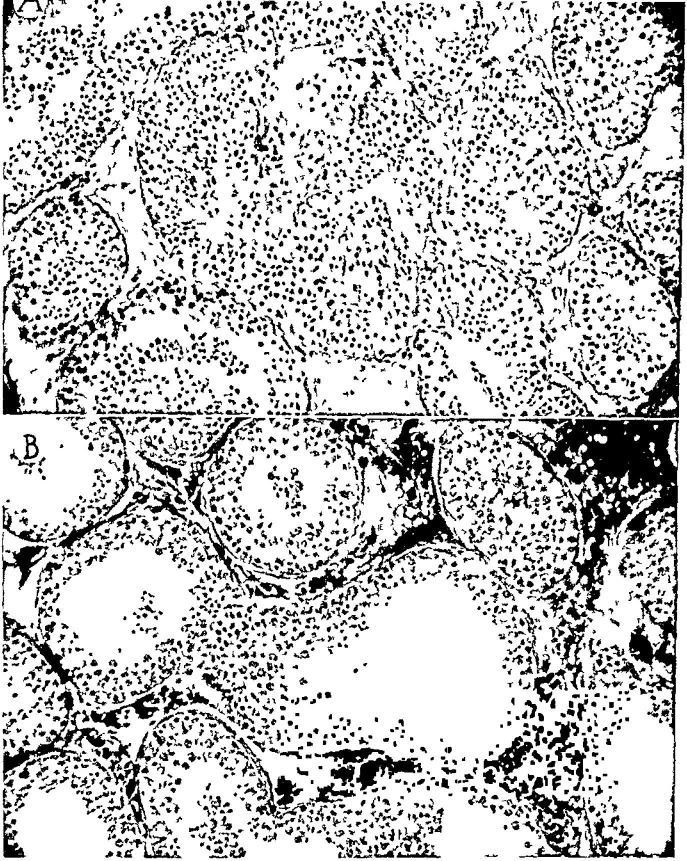

FIG 1 *A*, testicular biopsy of oligospermic man showing disorganization of spermatogenesis and sloughing of immature cells *B*, testicular biopsy showing incomplete germinal cell arrest predominately at primary spermatocyte level

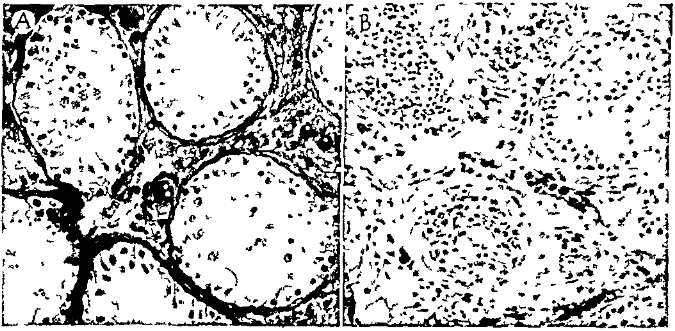

FIG 2 *A*, testicular biopsy showing germinal cell atrophy *B*, testicular biopsy showing extensive regional peritubular fibrosis

Eleven patients were originally azoospermic, and the condition was not altered by treatment.

In the 28 patients who exhibited the "rebound phenomenon," 20 pregnancies have been produced, resulting in 13 normal babies, 2 miscarriages, and one ectopic pregnancy.

Following our reports in 1951 and 1952,[3, 4] there was considerable skepticism as to the validity of this work. However, the work of Charny and Heller give additional evidence that a "rebound phenomenon" can be secured in carefully selected and properly treated oligospermic men.

The most important criterion for the effective treatment with testosterone propionate is the testicular morphology as determined by the pretreatment biopsy. At the present time we believe that this treatment is indicated in the men who are oligospermic, physically normal, and the testicular biopsy reveals changes of 1) disorganization of spermatogenesis with sloughing of immature cells (fig. 1, *A*), and 2) incomplete germinal cell arrest (fig. 1, *B*). Efforts to secure improvement in patients whose testicular biopsy revealed germinal cell atrophy (fig. 2, *A*) or extensive areas of regional fibrosis (fig. 2, *B*) have been disappointing.

Charny recently reported that treatment with testosterone propionate has produced spermatozoa in the ejaculate of a previously azoospermic man.[5]

CONCLUSIONS

Testosterone propionate is indicated in the treatment of patients who have an oligospermia when the testicular biopsy reveals a) disorganized spermatogenesis, or b) incomplete germinal cell arrest.

Testicular morphology is the most important criterion in determining the indication for treatment.

Twenty eight of 73 oligospermic men had a rebound in spermatogenesis exceeding 50 million in the total spermatozoa count. Following treatment, these patients have produced a total of 20 pregnancies in their wives.

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THE JOURNAL OF UROLOGY
Vol 75 No 6 June 1956
Printed in U S A

ARTIFICIAL INSEMINATION WITH TESTICULAR TISSUE EXPERIMENTAL STUDY

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In the study of infertile couples, there are some instances in which the woman is capable of having children, but the man has azoospermia, with a normal testicular biopsy In these instances, the cause of the azoospermia is a mechanical block in the genital duct system Many plastic operations have been performed on the vas deferens with mediocre success Another more obvious approach to this problem would be to directly implant testicular tissue in the female cervix This was done and reported by Adler and Makris[1] They report the case of a 24-year old man, married 5 years, with azoospermia, presumably a consequence of an earlier gonorrheal epididymitis In this case a biopsy was taken of testicular tissue (which contained living sperm), the tissue was then macerated in a cup of Ringer's solution This material was then placed in the cervix of the wife The wife missed her next period and subsequently, 9 months later, delivered a normal 8 pound infant To scientifically investigate this solitary report, the following investigation was carried out on rats

ARTIFICIAL INSEMINATION STUDIES

Method Using common laboratory white rats, repeated attempts were made to impregnate the female, using testicular biopsy tissue The female rats were impregnated only during the ovulation period, as determined by taking vaginal smears The male rats were first killed by means of a blow on the head and immediately the testes were excised and then carefully cut up into small fragments, placed in a container, and mixed with an equal amount of Ringer's solution One to two cubic centimeters of this emulsion was injected into the vagina of an ovulating female Two months after each of these tests (rat gestation is of 21 days' duration) a check of the fertility of the female was made by placing a male rat in the same cage with her to allow for nature to take its course and pregnancy to insue

Results Reference to table 1 shows that attempts to perform artificial insemination in rats, using macerated testicular tissue, were unsuccessful Most of the rats which were not made pregnant by artificial means, subsequently became pregnant after natural copulation with the male In three instances, an unsuccessful attempt was made to impregnate females, which had previously given birth to litters

DISCUSSION

Insemination using sperm from the testes apparently fails to impregnate the female Yet sperm obtained from an ejaculate specimen is routinely used and

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Accepted for publication December 5 1955

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TABLE 1. *Results of artificial insemination*

Date	Male Rat	Female Rat	Artifical Pregnancy	60-90 Days Later, Natural Pregnancy
April 7	1	1	No	Yes
April 10	1 & 2	2	No	Yes
April 20	2	3	No	Yes
April 26	3	4	No	Yes
		5	No	Yes
		6	No	Yes
April 27	4	7	No	No
		8	No	Yes
		9	No	Yes
May 7-12	5, 6, 7	10	No Artificial insemination daily for 5 consecutive days	Yes
May 17	8	11	No	—
May 18	8	12	No	Yes
July 1	9	2	No	Yes (previously)
		3	No	Yes (previously)
		4	No	Yes (previously)
July 6	10	13	No	—
		14	No	—
		15	No	—

often successful in inducing pregnancy. In these experiments, it was noted that spermatozoa obtained from the rat testis were less active than those seen in the epididymides and farther along the vas deferens. This leads one to the assumption that the testicular sperm are either immature or have not been subjected to some energizing substance which is elaborated in the duct system, somewhere along its journey from the testis to the urethra.

CONCLUSION

Artificial insemination with testicular tissue was unsuccessful in rat studies. Further attempts in humans might be warranted on an experimental basis, should suitable cases be found. Pending further positive results with the procedure one must be skeptical of its usefulness.

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THE JOURNAL OF UROLOGY
Vol 75 No 6 June 1956
Printed in U S A

URETHROCYSTOGRAPHY IN THE DIFFERENTIAL DIAGNOSIS OF PROSTATIC CANCER

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Any means of increasing the certainty of the diagnosis of prostatic cancer is welcome Where rectal palpation is uncertain only operative perineal biopsy provides a reliable diagnosis, and this involves considerable surgery All other methods involve quite an element of uncertainty, whether, in addition to palpation, they consist of endoscopy, transurethral biopsy, punch biopsy, acid phosphatase, or cytology of the urinary sediment Mistakes are possible in both directions

The systematic use of urethrocystography in the diagnosis of prostatic cancer has only been introduced in recent years, and its rôle is not yet fully established Investigations based on large materials have been published only by Edling (1948) and Moulonguet (1953) The correlation between clinical and roentgenological findings has actually not been described at all to date Elongation of the posterior urethra, its widening in the sagittal plane and the exaggeration of its normal angulation are features long considered peculiar to hypertrophy The typical appearance is termed by the French as sabre-like (*en lame de sabre*), but a less typical form even suffices for the diagnosis Carcinoma again has been characterized in brief by the narrowness, straightness and irregular contours of the urethra Many earlier authors hold that the diagnostic importance of urethrography is not great, and the roentgenology of prostatic cancer was not devoted many lines in the reports of the 1930's and 1940's

PRESENT INVESTIGATIONS

Material After going through all the urethrocystographies performed in our hospital in 1952–54, 77 cases were selected as qualifying for the present investigation They included 20 cases of carcinoma, 16 of which were histologically verified and 4 were absolutely certain on the basis of metastases etc Cases found to be benign on prostatectomy or autopsy (hypertrophies) totaled 16 The low number of the latter is explained by the fact that initially no routine urethrocystography was performed in clinically obvious cases of hypertrophy. Hence the number of clinically uncertain cases in the hypertrophy material may exceed the average Some of the remaining 41 cases were probably benign but as it was considered that no operation was indicated the diagnosis lacks verification Transurethral biopsy was performed in many of them but it cannot be considered to exclude cancer with certainty Thus the investigation is mainly based on a comparison of these 20 cases of carcinoma and 16 cases of hypertrophy

The *technique* was that of the customary radiography of the posterior urethra The bladder was filled with thin contrast medium, after which viscous water-

Accepted for publication December 5, 1955

soluble contrast medium was injected into the urethra by Knutsson's instrument. Anteroposterior and oblique films were made during the injection.

RESULTS

The very typical sabre-like posterior urethra in hypertrophy and, on the other hand, the typical rigid tube in cancer are readily recognizable, but these two findings by no means cover the bulk of the cases. Hence other indications of malignancy must be sought. The following additional properties have proved serviceable: the shape of the floor of the bladder, the contour of the posterior urethra, its width, its type of elongation, and its angulation.

Floor of the bladder. The normal prostate pushes the floor of the bladder some-

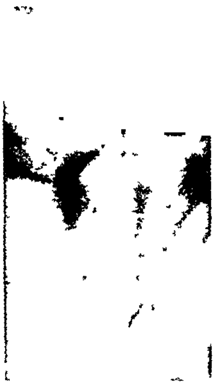

Fig. 1

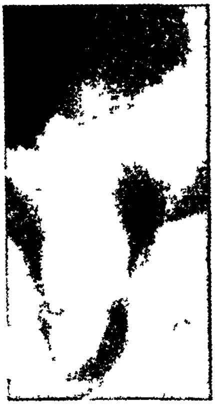

Fig. 2

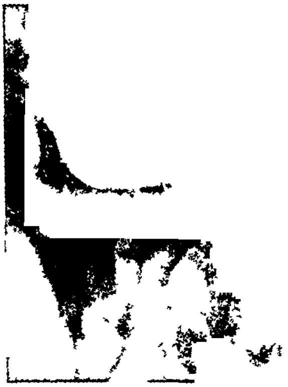

Fig. 3

Fig. 1. Hypertrophy. Oblique view

Fig. 2. Hypertrophy. Oblique view

Fig. 3. Cancer. Oblique view. Posterior urethra is narrow, rigid, ragged, not elongated.

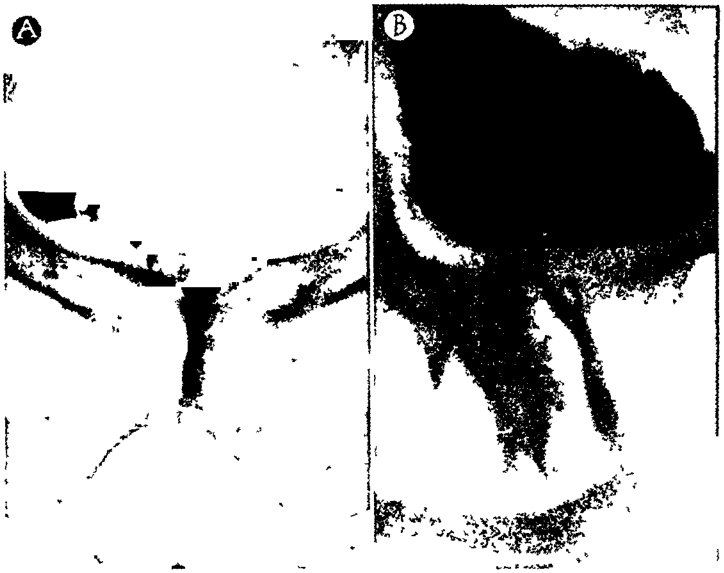

Fig. 4 Cancer. *A*, anterior view. Posterior urethra is laterally displaced and irregular Bladder floor irregular *B*, same case as *A*. Oblique view Posterior urethra is irregular, widened, rigid, straight Bladder floor irregular

what upward, depending slightly on the projection The enlargement of the prostate naturally results in enlargement of the prostatic impression In this respect the present material reveals no great difference between the benign and the malignant process Of greater importance is the contour of the floor of the bladder This refers to prostatic impression inside the bladder—when a sufficiently weak contrast medium is used—looming up as a semi shadow In hypertrophy the floor of the bladder is smooth or forms a few large, smooth nodes corresponding to the hypertrophic lobes In 2 hypertrophic patients only could the contour of the floor of the bladder be called irregular, whereas this symptom was present in 11 (55 per cent) of the carcinoma patients Prostatic carcinoma rarely causes an ulceration in the mucosa of the bladder, and hence the irregularity of the bladder floor usually takes the form of small nodes and does not show the ragged appearance of cancer of the bladder

The *contours of the posterior urethra* are practically always smooth in hypertrophy Even slight raggedness—not to mention large, irregular filling defects—is suspicious This does not refer to the gently sloping arcs due to asymmetric hypertrophy or an intraurethral median lobe Seventeen carcinoma patients (85 per cent) showed irregular contours of the posterior urethra In hypertrophy this symptom was present in only 3 of the 11 patients on whom no cystoscopies, repeated catheterizations or other intraurethral manipulations had been performed just before the x-ray examination Three of the five hypertrophy patients subjected to manipulations possibly traumatizing the urethra showed a ragged contour in the posterior urethra Hence *intraurethral manipulations seem to constitute an important source of error*, and urethrography should be the first examination performed Taking this source of error into account does not change the above percentage for the carcinoma patients

Widening of the posterior urethra in the sagittal plane was found with 11 hypertrophy patients (69 per cent) In 30 per cent of the carcinoma patients, too, the urethra was widened, possibly due to simultaneous hypertrophy. Widening—like other dimensions of the urethra—is difficult to express exactly, it must remain an estimate The normal diameter on oblique films is hardly more than 1 cm Narrowing is more difficult still to estimate, cancer causes no stricture proper The matter will be discussed in connection with the rigidity of the urethra

The *length of the posterior urethra* is usually but not always increased in both carcinoma and hypertrophy The normal measurements vary similarly to those of the parts of the posterior urethra Edling (1945) reported that the length of the supracollicular part was normally 1–1½ times that of the colliculus (verumontanum) In pathologic cases, the colliculus is often difficult to distinguish In those cases where some estimate could be made of the pars supracollicularis it was found to be elongated in 40 per cent of the carcinoma patients and 87 per cent of the hypertrophy patients Thus the normal length of the supracollicular part offers some evidence against benignity On the other hand, the length of the infracollicular part provided no guidance These factors are notably dependent on subjective opinions

Angulation of the posterior urethra. The normal posterior urethra is only slightly curved. In hypertrophy the bladder neck is often pushed forward, resulting in angulation with a fairly sharp or a gently sloping point. Mathey-Cornat considered a very acute point of the posterior contour of the angulation as a symptom of carcinoma, attributing the narrowness of the vertex (*en lame d'uréthrotome*) to an expansion of the infracollicular tumor. Nothing corresponding to this was found in our patients. An unusually sharp angulation was present in 63 per cent of our hypertrophy patients and only 25 per cent of our carcinoma patients.

A posterior urethra of stiff appearance is characteristic of cancer. The term refers to a urethra of nearly even width throughout, narrow, often elongated and fairly straight. Hence no precise concept is involved. Definite stiffness is an almost pathognomonic symptom as the posterior urethra of only one hypertrophy patient could be said to look stiff. However, the symptom was present in 11 (55 per cent) of the carcinoma patients; hence its absence is no evidence against cancer.

The sabre-like shape (elongated, sagittally widened and heavily curved posterior urethra) is also difficult to define exactly. In its typical form it was present in not a single of our carcinoma patients, and in only 4 of the hypertrophic cases (perhaps due to the selection of the hypertrophy material). Hence the very typical sabre-like shape speaks against cancer.

Other symptoms. Jomain and Moulonguet consider the indistinct contour of the posterior urethra important in cancer. They obviously do not refer to the ragged appearance. We were unable to find anything of this kind. The difference may be due to the fact that the above authors used lipiodol instead of water-soluble contrast medium. Moulonguet found several cases in which the posterior urethra was heavily dilated, even so much so that the external sphincter was indiscernible. We found nothing of this kind, any more than the large cavities in the prostate reminiscent of chronic prostatitis, reported by him.

Edling (1948) found that the whole posterior urethra was laterally displaced in carcinoma patients. In the present material the pelvis was often so much askew that the lateral deviation might just as well have been a parallactic phenomenon. Edling's investigation reveals, however, that a definite lateral displacement of the whole posterior urethra is strongly suggestive of malignancy. Anterior displacement is usually still more difficult to establish.

TABLE 1 *The correlation of urethrocystography with clinical and histological examination*

	Urethrocystographical Finding (No. of Cases)		
	Benign	Probably benign	Malignant
1. *Malignant cases* (histologically verified)			
Clinically malignant (11 cases)	—	1	10
uncertain (7).	1	—	6
benign (1)	—	—	1
2. *Benign cases* (histologically verified)			
Clinically benign (13 cases)	11	2	—
uncertain (3)	2	—	1

Malignant syndromes The more numerous and simultaneous the appearance of the above signs suggestive of cancer the greater is the probability of malignancy The cases in which a minimum of five signs indicated cancer included not a single benign case Five benign signs again, were shown by one carcinoma patient who nevertheless otherwise revealed an obviously malignant finding in the x-ray

Irregularity in both the floor of the bladder and the posterior urethra is an almost pathognomonic syndrome This combination was found with 50 per cent of the carcinoma patients but not once in hypertrophy, and the syndrome was present in only 2 of the 41 patients of our material whose prostate had not been histologically examined, both of them were also clinically suspect

Another obviously malignant roentgenological finding is *the absence of angulation combined with an irregular bladder floor or posterior urethra* It was established in 70 per cent of the carcinoma cases and not once in hypertrophy, excluding 2 patients with a traumatized posterior urethra This syndrome was present in 5 of the cases not verified histologically, two of them had prostatitis and one was suspect on palpation

These syndromes have not been described before

Clinical usefulness Table 1 shows that urethrocystography revealed the malignancy of one case not suspected at all clinically In eight out of 10 clinically uncertain cases it gave a correct classification into benign and malignant cases, in 2 cases it gave an erroneous finding (once in each direction) One clinically and histologically affirmed carcinoma gave a completely benign roentgenological finding

SUMMARY AND CONCLUSIONS

The authors list the symptoms considerably more often present in carcinoma than in hypertrophy, and report two roentgenological syndromes nearly pathognomonic of carcinoma Roentgen examination to verify prostatic carcinoma must be performed before any intraurethral manipulations are undertaken as even a slight traumatization due to the latter may simulate carcinoma Correctly performed and interpreted, urethrocystography can replace other examinations If the prostate is obviously malignant on palpation urethrocystography is no diagnostic aid In uncertain cases urethrocystography can often provide strong support for the decision, and in cases of benign appearance it may sometimes reveal a surprising carcinoma

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THE JOURNAL OF UROLOGY
Vol. 75, No. 6, June 1956
Printed in U.S.A.

RADICAL PERINEAL PROSTATECTOMY

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This report is an evaluation of some of our results with radical perineal prostatectomy. It is based upon a study of the records of 53 patients, most of whom have been submitted to perineal exposure of the prostate for frozen section biopsy and/or radical perineal prostatectomy.

Table 1 indicates the number of radical perineal prostatectomies performed by us over a period of 9 years. The average is 5 per year.

Table 2 was prepared a few years ago for a report on transurethral surgery. It contains a reference to radical perineal prostatectomy, indicating that 2.4 per cent of all our prostatic surgery is done for early, potentially curable, prostatic cancer.

Table 3 shows the age distribution of patients in this series. It is of interest to note that 17 per cent of these patients are in the sixth decade of life. This is a period of life in which increased endeavor should be made to find early lesions of prostatic cancer. Table 4 summarizes the data relating to diagnostic procedures. Rectal digital examination was reliable 75 per cent of the time. Frozen section biopsy was reliable in 93 per cent of the instances in which it was used. Transurethral prostatic resection corroborated our rectal digital examination 100 per cent of the time. By this we mean that in the 3 cases in which we thought carcinoma of the prostate gland was present, and moderately diffuse, transurethral prostatic resection secured adequate tissue for biopsy.

Table 5 shows the mortality statistics in this group. Of principal interest for this report is that no patient died as a result of the operation.

Table 6 gives some reassurance regarding postoperative control of urination. To our knowledge, no patient is totally incontinent or permanently dependent upon a device to protect him against leakage of urine.

Table 7 lists miscellaneous data which are of varying significance. The average postoperative stay in the hospital for these patients was 12 days. Five patients, or 11 per cent, in this group who have undergone radical perineal prostatectomy are able to perform sexually. Erections occur, intromission is effected, and orgasm is experienced. The fact that 18 of these patients, or 34 per cent, were seen simply because of the finding of a nodule or nodules, or areas of increased firmness in their glands, is most encouraging. These findings, without symptoms referable to the prostate gland, were sufficient unto themselves to prompt their physicians to refer them for opinion, advice, and treatment. More of this type of effort will result in the discovery and treatment of early prostatic cancer.

Table 8 summarizes the data relating to operative and postoperative complications. The rectum was opened early in the operation in four of these patients. It was recognized immediately and the opening was closed. The procedure was continued in each instance. No untoward developments occurred in these four.

Read at annual meeting, North Central Section of American Urological Association, Chicago, Ill. September 29–October 1, 1955.

TABLE 1 *Radical perineal prostatectomies done each year over a period of 9 years*

Year	Number
1946	1
1947	0
1948	2
1949	4
1950	6
1951	4
1952	6
1953	6
1954	13
1955	4
Total	46
Yearly average	5.1

TABLE 2

	Number	Per cent
Patients on whom prostatic surgery was performed	579	
Patients on whom transurethral prostatectomy was performed	555	95.8
Transurethral prostatic resections performed	593	
One stage transurethral prostatectomies	536	96.5
Two stage transurethral prostatectomies	18	3.2
Three stage transurethral prostatectomies	1	0.18
Suprapubic prostatectomies performed	10	1.7
Radical perineal prostatectomies performed	14	2.4
Operative deaths	0	

TABLE 3 *Distribution of patients in this series according to age*

Decade	Number of Patients
Sixth	8
Seventh	27
Eighth	11
Total	46
Oldest	75
Youngest	53
Average	65

Injury to the rectum, unrecognized, occurred in one situation and gave us our greatest trial of any of the patients in this series. Unilateral ureteral injury occurred in 1 patient. Perineal urinary fistula occurred in 2 patients. Rectovesical or rectourethral fistula occurred in 1 patient. Postoperative urethral stricture occurred in 11 per cent of these patients. The stricture, or narrowing, is usually at the site of anastomosis of the vesical neck to the membranous urethra. Fre

TABLE 4. *Summary of data by which diagnosis of prostatic carcinoma was confirmed or excluded (based on 52 cases)*

Method	Results	Percentage of Accuracy
Rectal digital examination	Carcinoma suspected in 48 cases; not suspected in 4 cases; unreliable in 13 cases	75
Frozen section biopsy	43 biopsies performed; 40 positive for carcinoma	93
Transurethral resection	3 resections	100

TABLE 5. *Mortality statistics*

	Number
Operative deaths	0
Deaths due to subsequent metastases	3
Deaths due to other causes	3

TABLE 6. *Postoperative control of urination (based on 44 cases)*

	Percentage
Immediate control	30.0
Control within 2 months	52.0
Control within 6 months	85.0
Control within 14 months	97.8

TABLE 7. *Miscellaneous data*

Postoperative stay in hospital	12 days
Postoperative sexual function	11 per cent
Patients referred for examination because of prostatic nodule, nodules, or unusual firm areas	18 (or 34 per cent)

TABLE 8. *Operative and postoperative complications (based on 46 cases)*

	Number	Percentage
Operative		
Rectal injury	5	11.0
Postoperative complications		
Perineal urinary fistula	2	4.3
Rectourethral fistula	1	2.2
Ureteral injury	1	2.2

quently after a few interval dilatations during the first year to 18 months following radical perineal prostatectomy, the stricture is no longer apparent, and additional interval dilatation is not necessary.

The diagnostic studies performed upon these patients consisted of rectal digital palpation of the prostate gland by at least two urologists, and in some instances three. Oftentimes the gland would be examined several times at intervals of a few weeks or a few months. Routinely a plain urogram is made and determinations are made of the serum acid phosphatase In the past year or two, determinations of the prostatic fraction of the serum acid phosphatase have also been made

The operation is usually performed under general anesthesia employing intravenous sodium pentothol, curare, and gas by the endotracheal route About 1500 cc blood is made available for use during the operative procedure and very frequently it is all used The approach to the prostate gland is the one described by Dr Elmer Belt The incision transecting the urethra, however, is made well distal to the prostatic urethra and no cuff of prostatic urethra and prostatic tissue is left The vesical neck is sutured to the membranous urethra employing a very small Mayo needle and 0 chromic catgut This single anterior mattress suture is, in our opinion, one of the most critical sutures, and should be placed very accurately in the vesical neck at 12 o'clock and in the membranous urethra at the same position Placing this suture well results in easy approximation of these two structures The rest of the anastomosis of the vesical neck to the urethra is then made with interrupted mattress sutures with a urethral catheter in place Otherwise the surgical procedure follows the Belt technique

Of the 53 patients operated upon, 43 had carcinoma of the prostate gland In the 43 carcinomas, the diagnosis was established in 33 by frozen section biopsy, in 7 by transurethral resection, in one by finding malignant cells in the prostatic secretion, and in two by routine paraffin sections

Three radical perineal prostatectomies were done for benign lesions In one instance the findings on rectal digital examination were considered diagnostic, however, the examination of the entire specimen revealed benign, cystic, glandular hyperplasia of the prostate In the second instance, the nodule removed for frozen section was reported to show cancer, but subsequent paraffin sections showed granulomatous prostatitis In the third circumstance, the patient, totally incontinent following two transurethral resections for benign prostatic hypertrophy, was operated upon in the hope that removing the scarred, fixed, prostatic urethra, glandular remnant and true capsule would improve his unfortunate situation The effort failed Seven of the 53 patients operated upon had nodules suspected of being malignant Frozen sections and subsequent paraffin sections revealed benign lesions Two of these were lesions of granulomatous prostatitis, one was chronic prostatitis, two showed benign cystic grandular hyperplasia of the prostate, one was benign cystic glandular hyperplasia with corpora amylacea, and one was normal prostatic tissue with corpora amylacea

Seven patients in this series had transurethral prostatic resection immediately prior to radical perineal prostatectomy In four of these, carcinoma was not suspected clinically In the four not suspected, the occurrence of the carcinoma was in multiple sections and not in a single isolated segment The 3 cases in which carcinoma was suspected clinically had lesions which we believed were confined within the prostatic capsule and therefore it seemed that these patients would stand a chance of being cured by radical perineal prostatectomy

It is of interest to note that three of the patients in this series had been operated upon several years previously and transurethral prostatic resections were performed. At the time of the resection, the prostate gland was clinically benign, and benign on microscopic examination. One of these patients had undergone transurethral resection 4 years previously; one, 4½ years previously; and the last patient, 3 years prior to the detection of a nodule in his gland.

Most urologists agree that the only cure for cancer of the prostate gland is radical prostatectomy. Some of the reasons why so few cures are obtained are:

1) The early lesion of prostatic cancer doesn't produce symptoms and therefore is not suspected until it has progressed beyond cure by radical surgery.

2) Some urologists believe that the complications of radical perineal prostatectomy are worse than the disease, and therefore they will not perform radical prostatic surgery.

3) Another important reason is that very frequently a conscientious examination of the prostate gland by rectal digital maneuver is not performed at least once a year on men over 50; or if the examination is performed and some questionable areas of induration are found in the prostate gland, these areas under question are not always accorded the significance which they deserve.

Summarizing again some of the data obtained from this study, one can state that an average of five radical perineal prostatectomies are performed by us each year. These constitute 2.4 per cent of our prostatic surgery. To date no deaths have resulted from the operation. The average age of the patient operated upon is 65. Thirty-four per cent of the patients operated upon for frozen section biopsy and/or radical perineal prostatectomy have no symptoms referable to the prostate gland. Frozen section is reliable 93 per cent of the time. Over 50 per cent of the patients have control of urination within 2 months following the operation. Eighty-five per cent have control within 6 months, and 98 per cent have control within 14 months. The average postoperative stay in the hospital is 12 days. Eleven per cent of these patients are able to perform sexually. Injury to the rectum occurring at the time of operation was noted in 11 per cent. Untoward reaction to this injury occurred in one patient, or in 2.2 per cent. Perineal urinary fistula occurred in 4.3 per cent, but healed with treatment. Rectourethral fistula occurred in 2.2 per cent, but healed with treatment. Ureteral injury occurred in 2.2 per cent, but was recognized early and corrected with no late complication.

Some conclusions can be drawn from this study.

1) The early lesion of prostatic cancer is asymptomatic, but can be suspected on rectal digital examination.

2) Urologists with good training in fundamental urologic surgery can perform radical perineal prostatectomy without taking special training.

3) Results of conservative palliative treatment of prostatic cancer are often striking and prolonged. It is better, however, to be living without cancer than to be living with one's cancer and under palliative treatment.

4) In our experience the complications following radical perineal prostatectomy are not significant enough to dull our enthusiasm for the procedure. Most patients are willing to accept the potential complications in order to be rid of cancer.

5) A willingness to investigate lesions of the prostate gland with the thoroughness which they deserve is stimulating to our colleagues, and they are thus apt to make a more thorough, frequent, and searching rectal digital examination of their patients

6) Although the technique of radical perineal prostatectomy is not difficult to learn, it would be far better if, in academic centers, more emphasis were placed on training in radical prostatic surgery The resident or fellow should emerge from his training with sufficient experience in radical prostatic surgery to give him enough confidence to perform the operation

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The Journal of Urology
Vol. 75, No. 6, June 1956
Printed in U.S.A.

HYPOTHERMIA INDUCED BY CYSTOSCOPY

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The usual cystoscopic procedure using irrigating fluids of room temperature can produce a significant hypothermia, especially in infants. Profuse irrigation of the relatively large and intra-abdominal bladders of small children can rapidly remove heat when the fluid is 18°C to 20°C below the body temperature. In practice, the additional cooling effect of ether anesthesia so frequently used, enhances the possibility of hypothermia.[1]

By simulating a cystoscopic examination in female dogs approximately the weight of infants under six months of age, the rapid production of hypothermia was demonstrated.

Two case reports of possible hypothermic reactions in a 7-week and 9-week-old infant following cystoscopy are reported.

CASE REPORTS

Case 1. A 9-week-old female child weighing 3200 gm. was admitted to the New York Hospital because of intermittent diarrhea and failure to gain weight. During hospitalization the diarrhea was controlled by dietary and medical means. On admission her blood urea nitrogen was 106 mg. per cent and on subsequent determinations was 65 mg. per cent, ranging down to a level of 30 mg. per cent where it appeared to stabilize. Because of three poorly visualized excretory urograms, a retrograde pyelogram was done approximately 1 month after the patient's hospital admission and at a time preceded by a 2-week period of excellent hydration and improving nutrition. Under open drop ether anesthesia cystoscopy and attempted retrograde pyelogram were undertaken for approximately sixty minutes. After 60 minutes of cystoscopy the child had generalized chills and a clonic convulsion. The procedure was terminated and it was found that the child's rectal temperature was 35°C, the skin cyanotic, the pulse 160, and heart tones were distant and weak. Within an hour the body temperature was normal and the child appeared entirely well. Four hours after this the rectal temperature was recorded as 41°C and returned to normal levels 3 hours later without chills or convulsions. It was thought that excess attempts to warm the infant following cystoscopy had accounted for the rise in temperature as the temperature remained normal from this time on and for the following seven days prior to discharge from the hospital.

The irrigation water used during the cystoscopy was at room temperature, approximately 21°C.

Case 2. A 7-week-old, white female infant weighing 4,650 gm. with a history

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Accepted for publication December 19, 1955.

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[1] Zeavin, I., Virtue, R. W. and Swan, H.: Cessation of circulation in general hypothermia. II. Anesthetic management. Anesthesiology, **15:** 113–121, 1954.

of recurrent fever, pyuria, abdominal distention and marked irritability was admitted to the Stanford Lane Hospital for urological investigation

The physical examination was otherwise normal and there was no other significant past history The patient was anesthetized with open drop vinethane and ether During anesthesia for 105 minutes, 75 minutes were consumed with the cystoscopic examination and radiological studies

Throughout this procedure no untoward reactions were noted with regard to the pulse rate, respirations, or general appearance One hour after cystoscopy the infant became cyanotic, with rapid, unobstructed respirations and a pulse of 140 to 150 per minute Respirations remained rapid and irregular, and rectal body temperature was recorded on several occasions to be between 34 8°C and 35°C for the ensuing 2 hours With the onset of oxygen and incubator care the shock-like state improved so that by 4 hours after cystoscopy, body temperature, skin color, pulse rate and respirations were entirely normal

Although it has not been conclusively proven that either of these post-cystoscopy episodes was a result of hypothermia following cystoscopy, it was this combination of hypothermia and circulatory collapse of very short duration that directed our attention to the possibility of hypothermia developing in infants during cystoscopy with cool irrigants

ANIMAL EXPERIMENTS

Four female mongrel dogs weighing 4 5 kg, 5 1 kg, 5 6 kg, and 5 3 kg, were anesthetized with intravenous nembutal and then maintained with inhalation ether Through a catheter placed urethrally into the bladder 100 to 200 cc of water, 20°C was left in the bladder 5 minutes, and then replaced with more of the same water This procedure was carried on for 60 to 90 minutes in each animal and from 1200 to 2500 cc of water was used to irrigate the bladder in each animal The room temperature range remained from 20°C to 21 5°C The dog's initial intragastric temperature ranged from 38 2°C to 38 4°C Both by the use of a mercury thermometer placed deep into the dog's rectum and by an intragastric electrically operated thermistor that rapidly changes in electrical resistance with small changes of temperature, the animal's body temperature was recorded All records of temperatures cited in this text were intragastric temperature, as the rectal reading was uniformly lower and was thought to be a regional rather than a true body temperature during and immediately after the bladder irrigations

A total of ten series of observations were made upon each of these animals with pauses of approximately one hour between each observation period to allow body temperatures to return to formerly normal levels

RESULTS

Figure 1 demonstrates the mean fall in body temperature recorded by the intragastric thermistor thermometer in all animals It was noted that after 70 minutes, bladder irrigations were stopped and the bladder allowed to remain empty For the next 15 to 30 minutes the body temperature continued to fall so

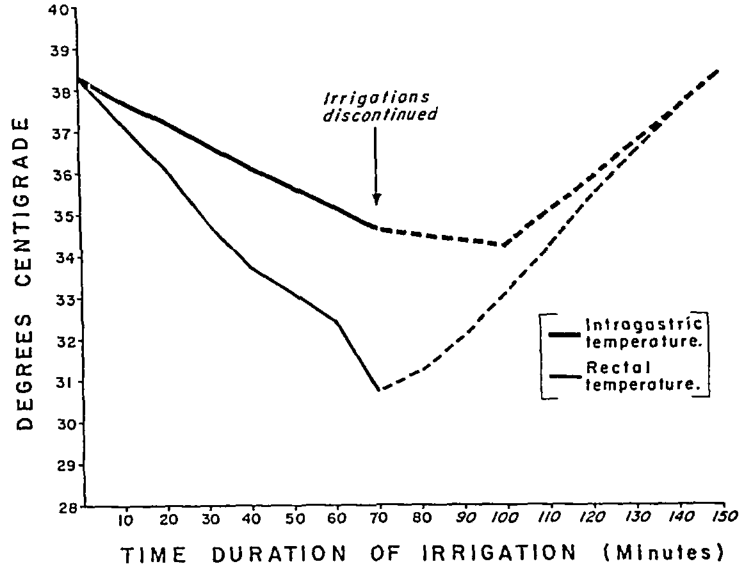

Fig. 1. Changes in dog's temperatures with bladder irrigations. Room temperature 20–21.5°C. Anesthesia—intravenous nembutal and ether.

that 30 minutes after the cessation of irrigations the mean fall in body temperature was 4.1°C. This observation, the continued fall in body temperature after the causative agent is discontinued, is a common one in hypothermic experiments and is the result of equilibration with regional cooler area. In this case, the pelvis and lower abdomen equilibrated with the rest of the body. The rectal temperatures recorded varied with the depth to which the rectal mercury thermometer was placed. The mean fall in rectal temperature taken 15 to 20 centimeters within the rectal canal was 7.6°C. The greatest fall in intragastric temperature in one animal was 5.1°C and the least was 3.0°C. It was noted that as the intragastric temperature continued to fall for 15 to 30 minutes when the irrigations were discontinued, the rectal temperature started to rise at approximately the same rate. By 45 minutes after the cessation of irrigations, the mean body temperature had risen 1.1°C from the lowest levels and continued to climb so that in approximately one hour the animals' body temperature was within 0.2°C of its starting temperature. At this time another series of irrigation and temperature observations was done on all of the dogs.

On six trials, intragastric temperature was recorded under similar anesthetic conditions with no bladder irrigations. No fall in temperature greater than 0.2°C occurred and there was no temperature change in three of the trials.

On eight trials, intragastric temperature was recorded under identical conditions using water introduced at the dogs' normal body temperature. No fall or rise in temperature greater than 0.3°C occurred and there was no change in five of the trials.

Observation in 4 children under six months of age weighing 5.3 kg., 6.3 kg., 8.1 kg., and 9.1 kg., during cystoscopy using water 20°C for periods under one hour demonstrated no rectal temperature fall greater than 0.9°C with a mean fall of 0 5°C These observations were secondary to clinical cystoscopy and accordingly control of irrigation time and amounts, and length of procedure was not possible It is significant that the greatest fall in body temperature occurred in the smallest child of this group

We have occasionally noted postoperative drops in body temperature in the 24- to 48-hour period following transurethral resection of the prostate A review of 100 random selected cases of these revealed no causal relationship between any body temperature changes and cystoscopic irrigant temperatures For such a relationship to exist, a fall in temperature after using a cool irrigant would need to occur during or shortly after such a procedure Fall in temperature 24 to 48 hours after transurethral resection was probably related to blood loss or shock from other causes.

DISCUSSION

Although artificially induced hypothermia is being used as an adjunct to the anesthetic management of the patient for intracardiac and other types of surgery, the hypothermic patient is subject to many significant physiological variations from the normal The hazards of ventricular fibrillation and other unpredictable cardiac manifestations are well recognized in some hypothermic patients [2]

Bergstrand and Sterky described notable, though reversible, decreases in glomerular filtration and renal plasma flow with hypothermia [3] Decreased oxygen consumption during hypothermia, decreased oxygen carriage, decreased pulse rate, and decreased respiratory rate during hypothermia have all been described by numerous investigators [4, 5] Both clinical cases reported here however had increased pulse rates during the hypothermic episode Several studies have shown a constant fall in the serum potassium levels during hypothermia [6]

After an initial rise associated with the period of shivering both cardiac minute volume and oxygen consumption was found to decrease by other studies [7] The plasma volume of dogs subjected to immersion hypothermia was shown to be diminished by as much as 12 per cent [8] Arterial blood pH has been shown to fall with an inverse linear relationship between hydrion concentration and body temperature down to 25°C

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[2] Hegnauer, A H Shriber W J Haterius, H O Flynn H O and Wolff R Cardiovascular response of the dog to immersion hypothermia Am J Physiol, **161** 455 465, 1950

[3] Bergstrand, A and Sterky, G Renal function in hypothermia Acta Physiol Scand, **31**: 13-21, 1954

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[5] Bigelow, W G, Lindsay, W K, Harrison, R C Gordon, R A and Greenwood, W F Oxygen transport and utilization in dogs at low body temperatures Am J Physiol, **160**. 125-137, 1950

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[8] D'Amato, H E and Hegnauer, A H Blood volume in the hypothermic dog Am J Physiol, **173** 100-102, 1953

[9] Cranston W I, Pepper M C and Ross, D N Blood reaction during hypothermia J Physiol (London) **125** 20-1P 1954

Although most of the physiological variations just described have occurred at hypothermic levels lower than we could develop in dogs with bladder irrigations, the changes described have a linear relationship to the degree of hypothermia and therefore occur in the dog or infant with only three or four centigrade degrees of hypothermia.

During the course of cystoscopy in infants other factors are present which can further lower body temperature. Anesthesia has been shown to facilitate hypothermia and hyperventilation can produce cooling as much as 10°C if continued long enough.[1] The absence of a fully developed heat regulatory mechanism is well known in infants and is a major reason why care should be taken to maintain their body temperature homeostasis. Many experienced pediatric surgeons emphasize that body chilling should be avoided during operations and transportation to and from the operation room.[10]

SUMMARY

Bladder irrigations, as in cystoscopy, with irrigants at room temperature can reduce the intragastric body temperature of a small dog as much as 4.5°C in an hour.

Two cases of hypothermia and circulatory collapse in infants are described which may be secondary to cystoscopically induced hypothermia.

A more physiological state with regard to oxygen carriage, oxygen consumption, cardiac rate, circulatory blood volume, and renal plasma flow can be maintained with the use of cystoscopic irrigation fluid at or near body temperature and thus prevent hypothermia which might otherwise be produced with cooler irrigants.

The author wishes to express his appreciation for the guidance of Dr. Henry M. Weyrauch in the preparation of this paper and to thank the Brady Urological Foundation of the New York Hospital, and Dr. William A. Sumner, Stanford Lane Hospital for permission to cite the case histories discussed.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 6, June 1956
Printed in U.S.A.

REACTIONS DUE TO INTRAVENOUS UROKON

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Urokon was introduced several years ago as a commercially prepared contrast medium for excretory urography.[1, 2] Its acceptance has been widespread by the fact that more than two million ampules have been sold.

There seems to be general agreement among urologists that reactions with urokon are more frequent than was originally thought. It has further been suggested that reactions with urokon are more common than reactions to the older drugs used for contrast studies. Pendergrass's[4] analysis of twenty-seven sudden deaths occurring in the United States since 1942, from intravenous contrast media, included 1 case from 30 per cent urokon. This report is concerned with 2 cases, a death from 70 per cent urokon and a severe reaction from 50 per cent concentration of the same drug.

CASE REPORTS

Case 1. Mr. J. S. (CMH No. 108812), a 60 year old white man, was admitted to the Cabarrus Memorial Hospital on June 1, 1954, with a history of hematuria for 3 months associated with a weight loss of 15 pounds. On the day prior to admission cystoscopy performed in the office revealed a tumor in the dome of the bladder adjacent to a diverticulum.

General physical examination was essentially unremarkable except for blood pressure of 160/90, a grade 2 apical systolic murmur and slight suprapubic tenderness. The past history was negative except for broken bones on two occasions and a cellulitis of the hand during the 1930's which was treated by some type of sulfonamide with a resulting skin "reaction" which cleared following cessation of the drug.

On the morning following admission, the patient was referred to the x-ray department for chest x-rays and excretory urography. One hour before going to the x-ray department 50 mg. pyribenzamine had been given orally. Prior to x-ray studies the patient was questioned about allergy and his answers were all negative. One cubic centimeter of 70 per cent urokon was injected into an antecubital vein without reaction and 2 minutes later the remaining 24 cc. were injected in about 3 minutes time. The patient gave no immediate complaints. The technician left the x-ray room to change cassettes and upon returning

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Accepted for publication December 13, 1955.

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[2] Mullen, W. H., Jr. and Hughes, C. R.: Intravenous urographic contrast media. Controlled study of diodrast and neo iopax. Am. J. Roentgenol., 69: 903, 1952.

[3] Pearlman, C. L. and Newland, J. E.: Severe reaction due to intravenous neo iopax. Case report. J. Urol., 68: 407, 1952.

[4] Pendergrass, E. P., Hodes, P. J., Tondreau, R. L., Powell, C. C. and Burdick, E. D.: Further consideration of deaths and unfavorable sequelae following administration of contrast media in urography in the United States. Am. J. Roentgenol., 74: 262, 1955.

approximately two or three minutes later, found the patient unconscious, cyanotic, and partially off the x-ray table.

Less than one minute later, one of the authors (V. H. Y.) was present and found the patient cyanotic; oxygen was started and the patient's false teeth were removed and his tongue pulled out and a satisfactory exchange was brought about. A tracheotomy tray was ordered and was available within a minute or two. Another physician was preparing to do a tracheotomy but the cyanosis rapidly disappeared and the patient breathed slowly but spontaneously. Oxygen was administered by anesthesia machine.

Throughout this time the patient's pulse was good, although he remained unconscious. About five minutes after the apparent onset of the reaction, the patient's blood pressure was 130/70, he began to move about as though he was regaining consciousness and his pulse was much stronger. An assisting physician believed that the patient was entirely out of danger and left the x-ray department. Suddenly the patient stopped breathing, it was impossible to exchange oxygen by artificial respiration or with the anesthesia machine and an intratracheal tube was passed through an edematous larynx. The patient became rapidly cyanotic, pulseless, and no heartbeat could be ascertained and he was pronounced dead approximately 20 minutes after the first injection of urokon.

Drugs used during this time were intravenous benadryl and finally when the patient appeared to be terminal, coramine and adrenalin were given intravenously and directly into the heart without effect.

An autopsy was obtained and performed approximately one hour after death. The positive gross findings were confined to the larynx, posterior nasopharynx, and to the urinary bladder. The larynx was soft, markedly edematous, and the capillaries were congested with red blood cells. In the posterior nasopharynx there were extremely large, edematous, soft blebs of material immediately beneath the mucosa. The swelling from these edematous areas appeared grossly to have been enough to occlude the air passages. Immediately beneath the pharynx the trachea was filled with tenacious, thick, mucoid material which extended to involve the entire trachea and portions of both right and left main stem bronchi.

The urinary bladder showed a diverticulum on the right side of the dome of the bladder, which was 5 cm. in diameter and 2 mm. in thickness. Inside this diverticulum, there was a distinct polypoid-shaped structure which measured 3 cm. in length, 2 cm. in diameter, and was attached by a 1 cm. pedicle to the dome of the diverticulum. This was a fungating, papillary growth which microscopically conformed to the criteria for a papillary adenocarcinoma.

The prostate gland was moderately enlarged and showed minimal nodular hyperplasia. Otherwise the organs of the body were entirely unremarkable, including the brain.

In addition to this case being important from the standpoint of urokon administration, it is quite unusual for adenocarcinoma to be observed in the bladder which arises in a diverticulum. This is an extremely rare occurrence;

in fact, there are many who doubt that primary adenocarcinoma of the urinary bladder actually occurs. It may, of course, be present as a metastatic lesion. However, in our patient all possible sites of metastasis were grossly and microscopically ruled out. This tumor probably arises either from enteric rests or from remnants of the cloaca, or perhaps remnants of the urachus. This particular type of tumor has been adequately discussed by Kretschmer[5] and Hurwitz.[6]

In the absence of other findings, both grossly and microscopically, we felt compelled to refer to this case as congenital anaphylactic reaction due to urokon. This term may leave much to be desired. It was believed, however, that it best explained the particular phenomenon which this patient presented. By using this term, we mean to say that this patient was apparently born with some specific sensitization to one or more of the elements that are present in the urokon, as he has not been previously sensitized to this particular drug and therefore would represent a congenital sensitivity.

Comment. The foregoing case report is an instance of congenital anaphylaxis due to conjugated iodine contained in the urokon. A later history obtained from the patient's wife revealed the allergic history to be negative except for the reaction to a sulfonamide seventeen years before. There was no family history of allergy. It was also stated that tincture of iodine had been a common household antiseptic for cuts and abrasions received in the patient's work as a carpenter.

Following that catastrophe, patients who received 70 per cent urokon were more closely observed. The instances of nausea, flushing of the face, fullness in the chest, etc., were no higher with urokon than with other contrast media. There was, however, an increased tendency to thrombosis of the arm veins which appeared as early as one day and as late as two weeks following injections. The patients complained of a sore arm and in several cases, small doses of narcotics were required to relieve pain. In all patients followed the "cord-like" consistency of the vein and pain disappeared rapidly with only one persisting for nearly three months.

When 50 per cent urokon became available, this was substituted as the standard contrast medium for excretory urography; however, neoiopax and diodrast were also used frequently, usually on a physician's specific request.

An emergency kit containing a tank of oxygen with a mask and bag, intravenous and intramuscular hydrocortisone, intravenous benadryl, throat gag, tongue forceps, and suction apparatus was prepared and placed in the x-ray department. In addition, 0.5 cc of 1:100 adrenalin and 10 mg. of intravenous chlortrimeton were drawn up in separate syringes, their needles wrapped in an alcohol sponge, and kept directly adjacent to the x-ray table. From June 1, 1954 until July 21, 1955 there were no reactions severe enough to require the use of emergency measures. During that time approximately 850 excretory urograms were made, with urokon in the majority of cases.

Case 2. Mr. K. C. (CMH No. 121248), a 66-year-old farmer, was admitted to the hospital for an elective transurethral resection. The patient had been first seen in December 1951 with acute prostatitis and at that time mild prostatic obstruction was noted but no resection was deemed necessary. Four weeks prior to the present admission, the patient had acute prostatitis which once again responded to conservative therapy. After subsidence of all symptoms, the residual urine was 30 cc; mild symptoms of prostatism were present. Endoscopy revealed marked blockage of the prostatic urethra by secondary bladder signs. The patient was admitted to the hospital and a preliminary excretory urogram ordered.

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[6] Hurwitz, S. P., Jacobson, E B. and Ottenstein, H. H.: Mucus adenocarcinoma of urachus invading bladder. J. Urol., 65: 87, 1951

The patient gave a history of having "some type of reaction to an anesthesia" in a Richmond, Virginia Veterans Hospital some years ago while undergoing cholecystectomy. The nature of this reaction was unknown. Otherwise his personal and family history for allergy were entirely unremarkable.

On July 21, 1955 the patient was taken to the x-ray department where a skin test with urokon was read as negative. A plain x-ray was unremarkable. The technician was unable to locate a vein and the patient returned to his room for approximately two hours until the author (V. H. Y.) could come to the x-ray department and give the 50 per cent urokon. The remaining 24 cc were slowly injected. There was no immediate reaction but about three minutes later the patient complained of a peculiar taste in his mouth, followed immediately by a flushing of the face and a desire to vomit. The patient attempted to turn his head to vomit and immediately began to froth at the mouth; there were generalized clonic convulsive movements of the body, he became slightly cyanotic and no respiration was noticed. Immediately artificial respiration was started, the pulse was found to be good; adrenalin 0.5 cc was injected subcutaneously and chlortrimeton 10 mg. injected intravenously. After about five or six compressions of the chest, the patient began to breath spontaneously, the pulse then became imperceptible for about two minutes. Then the patient's blood pressure rose rapidly from a systolic of about 60 to 110 two minutes later. Oxygen was given by mask throughout the entire procedure. Approximately four minutes after the convulsive movements he became conscious and was groggy but was aware that something unforeseen had happened to him. Benadryl 50 mg. was injected intravenously. Routine pyelograms showed poor concentration and poor function. The patient remained groggy and complained of malaise and generalized body aches throughout the rest of the day but felt well the following day. The non-protein nitrogen value was 31 mg. per cent on the day of the reaction and when repeated the following day was unchanged.

An electrocardiogram made after the reaction was essentially the same as one done several weeks previously in an internist's office. The patient subsequently had a transurethral prostatic resection complicated by the development of right epididymitis which occurred in spite of ligation of the vas deferens.

DISCUSSION

Excretory urography is not without reactions and can never be considered as entirely innocuous. The information obtained from this procedure is of such value that it is unlikely that it will be abandoned or even restricted Pendergrass[4] reports twenty-five immediate deaths in a study of 3,831,850 urographic examinations One of these deaths was due to the injection of 20 cc of 30 per cent urokon The patient was a 48-year-old man who was referred because of lumbar pain After the injection of the contrast medium, he fainted several times and was removed to a hospital and died 2 hours later during a convulsion An autopsy was not done Pendergrass[4] further states that of 15 patients who died immediately after injection of contrast medium, negative tests for sensitivity were obtained In six other cases, tests were not done and there was no record on 4 cases It is his opinion that sensitivity tests cannot predict a fatal reaction but a more careful clinical history with regard to allergy combined with clinical judgement gives the most reliable basis for a decision to use intravenous contrast media

Only two hundred cases of carcinoma arising from a diverticulum of the bladder have been reported and of these only three have been adenocarcinoma[7] The fourth case is reported as an incidental autopsy finding following death from urokon

SUMMARY

A case of anaphylatic shock resulting in death and a case of severe reaction with recovery, both from intravenous urokon, are reported pain. Since benadryl is an antihistaminic and aids in dissipating allergic phenomena, our findings suggest that nausea, vomiting, taste and arm pain are not allergic reactions to contrast media.

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[7] Cooney, J D , Amelar, R D and Orron, A Adenocarcinoma arising in diverticulum of urinary bladder A M A Arch Surg , 69 752, 1954

Because 50 mg. of intravenous benadryl produces drowsiness in some patients, all patients are advised not to leave the hospital unescorted following pyelography.

SUMMARY

No urticarial, asthmatic or shock-like reactions were observed in 1,281 consecutive patients receiving intravenous benadryl immediately prior to injection of 70 per cent urokon.

Addendum: Recently the 1500th patient exhibited urticaria and bronchospasm.

THE JOURNAL OF UROLOGY
Vol 75 No 6 June 1956
Printed in U S A

A SIMPLE METHOD OF RETAINING CATHETERS

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A number of methods have been used to retain catheters[1] [2] [3] This retainer is not new in principle However, in institutions where a large number of nephrostomy, pyelostomy or ureterostomy catheters are in use, this retainer can be easily and inexpensively made by a technician It is used for whistle tip-like catheters which at the Paraplegic Center are preferred to the self-retaining catheters for nephrostomies, pyelostomies or ureterostomies It can also be used for suprapubic whistle-tip catheters We have found it easier to use a rubber retainer rather than plastic since it molds better to the particular contour of the body Rectangular shaped retainers have been used rather than round but any shape can be made

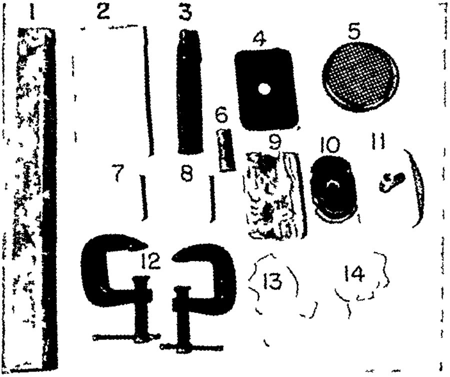

FIG 1 Integral parts of nonwelded "catheter retainer making" setup

Figure 1 shows the necessary parts used by T T The ruler is used to give approximate sizes The items are *2*, hard rubber (used as a flat surface for boring holes), *3*, steel "hole" punch, *4*, cold patch, *5*, rougher, *6*, proximal end of an "old" rubber catheter or rubber tubing, *7 and 8*, plywood blocks, *9*, plywood plate with center hole, *10*, hot patch, *11*, finished retainer, *12*, two small C clamps (size 1½ inches), *13 and 14*, heavy nylon thread used to place around No 6 when retainer is placed over catheter

Figure 2 demonstrates the method of placing the cold patch, catheter end, and hot patch together

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Accepted for publication December 5, 1955

[1] Bardam suprapubic retainer and Breakey Burhans nephrostomy retainer Urological Instruments C R Bard Inc , Summit, N J , 1952, pp 33, 37

[2] Palken, Morton A plastic holder for nephrostomy tubes J Urol , 69: 465–466, 1953

[3] Retention discs Urological and Allied Diagnostic Instruments and High Frequency Equipment American Cystoscope Makers, Inc , New York, N Y , 1952, p 198

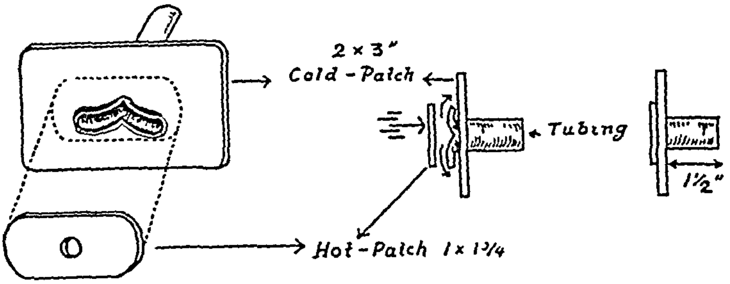

FIG. 2. Ureterostomy, pyelostomy, nephrostomy and suprapubic retainers. Method of placement of cold patch, catheter end and hot patch

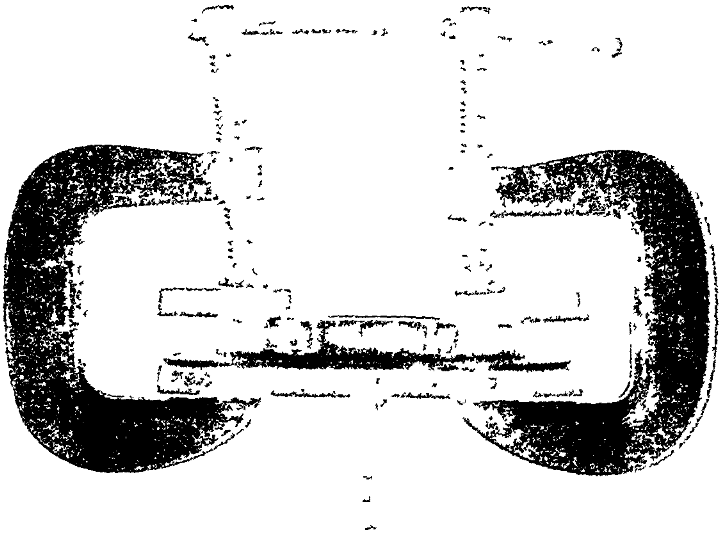

FIG. 3. Setup ready for lighting of hot patch. Here wooden plates are used

Figure 3 shows the apparatus, using detachable wooden plates, ready for lighting of the hot patch.

Since it is somewhat cumbersome to handle the individual parts, the apparatus shown in figure 4, *A* was developed. This consists of the integral parts being welded to the C clamps. A groove has been cut into the metal base ⅝ inches wide. Five metal plates have been made available in the center of which have been drilled holes measuring ⅜ inch, $\frac{7}{16}$ inch, ½ inch, $\frac{9}{16}$ inch, and ⅝ inch respectively. These plates are adequate for the variety of sizes of catheters that will be used. To the desired size of metal plate are fixed the cold patch, catheter end and hot patch. The plate in turn is slipped through the groove depicted in figure 4, *A*. The entire system is tightened and figure 4, *B* shows the final setup ready for lighting of the hot patch.

After cooling, the retainer is sterilized and ready for use.

Figure 5 demonstrates our method of using elastoplast and ties in order to hold the retainer in a fixed position. A split 4 by 4 inch gauze pad is placed between the skin and rubber retainer and also between the retainer and the elastoplast. The gauze may be changed daily or as required; and the catheter and retainer are

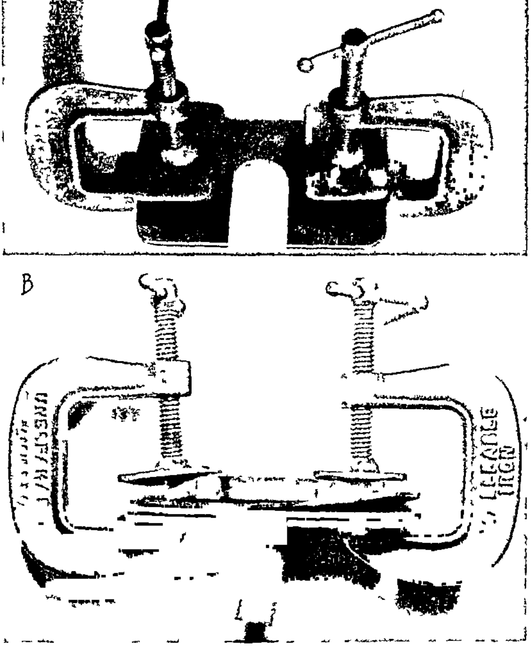

FIG 4 *A*, metal plates welded to C clamps Metal base, with $\frac{5}{8}$ inch diameter groove, measures 2 by 3 inches Two "tightening" plates measure 1 by 1½ inches *B*, setup ready for lighting Setup has welded metal plates

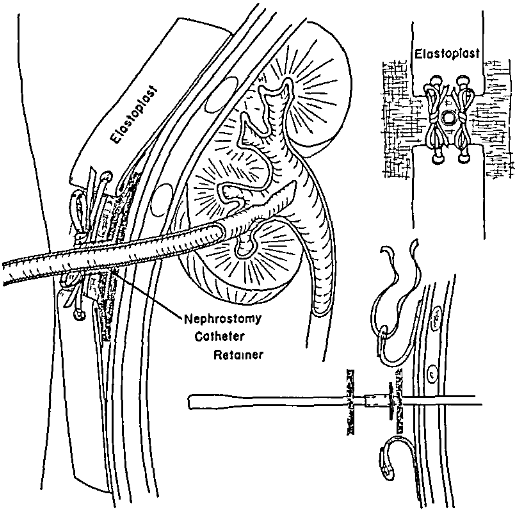

FIG 5 Method of holding "catheter retainer" in position

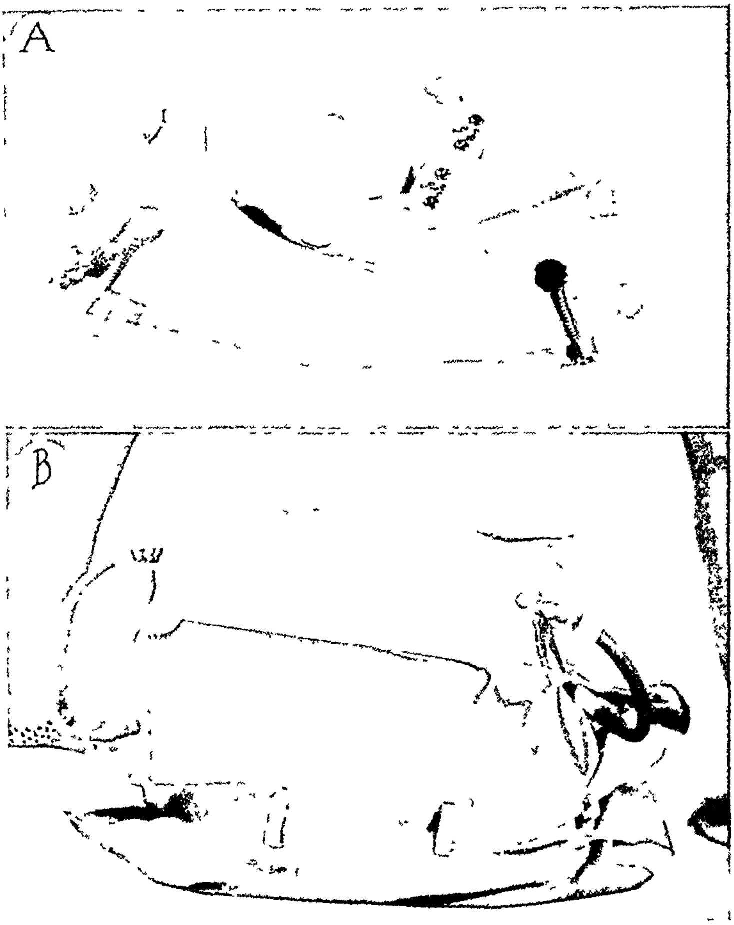

FIG. 6. *A*, additional method of holding "catheter retainer" in position. *B*, catheter retainer acting as "girdle " "Zipper" makes application simple.

changed weekly. If infrequent dressings are performed, elastoplast strips can be placed across both sides of the retainer and onto the skin. This latter procedure depends on the skin's tolerance of elastoplast.

At surgery, nephrostomy catheters are held in position with wire sutures to the skin until the time when the wound is healed and a good nephrostomy channel has been formed. Only then is the retainer used as described.

For additional safety, some patients, especially with bilateral nephrostomies, prefer to use, in addition, a 6 inch elastic belt with holes to permit the exit of the catheters. This "girdle" reinforces the retainers and is also excellent as a support if postoperative muscle weakness is present (fig. 6).

SUMMARY

A simple, inexpensive method of making nephrostomy, pyelostomy, ureterostomy or suprapubic retainers has been described. A very satisfactory method of keeping the "catheter retainer" in place is presented.

THE JOURNAL OF UROLOGY
Vol 75, No. 6, June 1956
Printed in U.S.A.

AN AID FOR THE MAINTENANCE OF STERILITY OF DRAINAGE TUBES

WILLIAM E. FORSYTHE, PAUL J. STEUBER, JR. AND
MARGARET H. HAMILTON, R.N.

The desirability of early and frequent ambulation of urological patients is well established and commonly practiced. Various methods used to care for the connecting tube and catheter plug during irrigation of the catheter, or ambulation of the patient, have allowed frequent accidents and contamination of the constant drainage apparatus. The errors in handling the tubing concern the urologist, the sterility of the system, and even occasionally the patient.

In our practice, we encourage the patient to walk with the urethral or suprapubic catheter occluded by the common plastic plug, since clamping of the catheter by a hemostat or screw clamp is damaging to the catheter and frequently increases the possibility of infection.

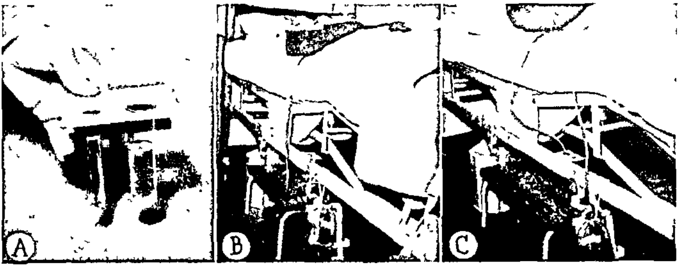

FIG. 1

When the catheter is reconnected to the drainage system, the plug must be kept in sterilizing solution, easily accessible to nurse, house officer and patient. At the same time this container should NOT be on the bedside stand.

An apparatus (figs. 1 and 2) was developed from an idea of Mrs. Margaret A. Hamilton of the Central Supply Division of Euclid-Glenville Hospital in Cleveland, and has been enthusiastically used during the past year. It consists of a metal rack which fits over the side frame of the modern hospital bed. Into this rack fit two pyrex, lipped, test tubes containing an antiseptic solution (either mercuric cyanide or bichloride of mercury). The larger tube will accommodate the adaptor of the drainage tubing. The smaller test tube will allow the cone-shaped part of the plastic catheter plug to rest in the solution with the handle protruding above the lip of the test tube.

The metal part of this rack can be easily made into the desired shape by the hospital maintenance department, or a local metal fabricating shop. The holes are drilled to allow the tubes 25 by 100 mm. and 12 by 100 mm. to rest on their

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Read at annual meeting, North Central Section of American Urological Association, Chicago, Ill. September 29–October 1, 1955.

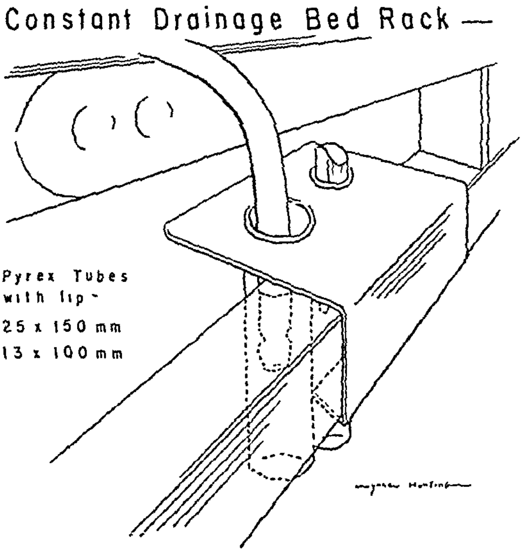

FIG. 2

flanged lips. The test tubes are easily replaced if broken and the rack is easily removed from the bed if no longer needed.

When the rack is in position on the bed, there are no projections beyond the bed frame, thus preventing the holder from being struck by doorways or by the tibial surfaces of the personnel. Yet, the modern bed allows several inches of clearance between springs and frame, making insertion of the connector and removal of the plug easy for even the patient himself at the time of ambulation.

SUMMARY

We have presented a simple, inexpensive metal rack with test tubes, that has facilitated the care and improved the sterility of urinary drainage tubes and catheter plugs.

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THE JOURNAL OF UROLOGY
Vol. 75, No. 6, June 1956
Printed in U.S.A.

ALTERATION OF THE McCARTHY CYSTOSCOPE TO PERMIT USE OF THE MEAD TELESCOPE

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Urologists still dream of the universal cystoscope. Although we do not expect to achieve this elusive end, we keep trying. Occasionally it is possible to modify one instrument for use with another, and it is the purpose of this paper to tell of such an instance.

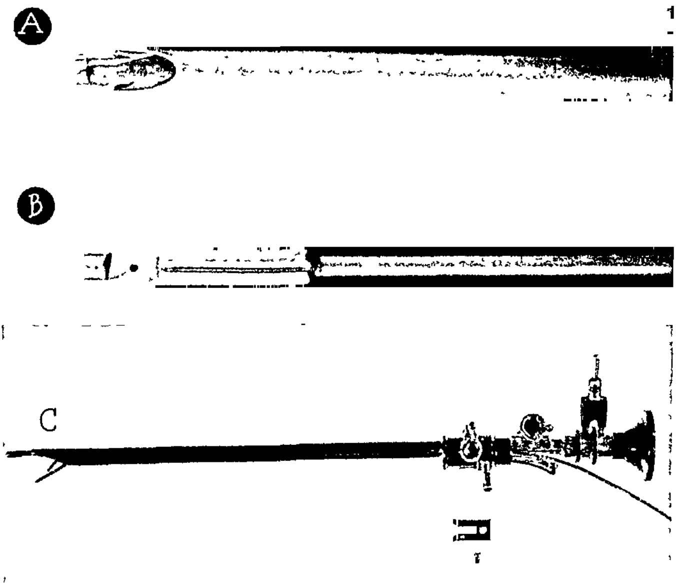

FIG. 1. *A*, alteration of McCarthy sheath by filing tip. *B*, obturator altered. *C*, instrument assembled.

For those who use the McCarthy routine cystoscope there arise periodically occasions when the right angle type of instrument with a deflector would be useful. This occurs particularly when coagulating tumors found on the dome of the bladder or on the anterior or high lateral walls. Also, there are some cases of large prostatic hyperplasia where ureteral catheterization is impossible without a deflecting mechanism. Until the present time it has been necessary to change

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Read at meeting of North Central Section of American Urological Association, Chicago, Ill September 29–October 1, 1955.

instruments and introduce a Brown-Buerger cystoscope on these occasions. To avoid this nuisance, a right angle telescope with deflector was ordered from American Cystoscope Makers, Inc. When received it was found to be a telescope which, while it had a deflector, had a foroblique lens system with its characteristic forward field of vision. Since this was not what was wanted it was returned.

Having used the Mead telescope many times, we inspected it again with the idea of seeing how much alteration would be necessary and with the intention of having made a special telescope of similar construction. Inspection showed that the length was all right and that it would fit the 24F and larger sheaths after removal of the small locking lug. The telescope was slightly bent, however, to pass the bead on the thick, blunt tip of the beakless sheaths. This bead is easily filed out so that the telescope fits quite nicely, although it does not lock in position. V. Mueller and Company altered our sheaths in this manner (fig. 1, *A*) and also altered the obturators to fill out the defect (fig. 1, *B*). It is not necessary to alter the beaked sheaths, since the bore is full size to the very end. This telescope has worked very well under these conditions and on many occasions has saved both time and inconvenience for the operator, and discomfort for the patient.

The absence of the locking pins on the hub has not been troublesome; one quickly gets in the habit of holding the parts together with the holding hand as one does in resection. The small locking lug can be quickly replaced for use with resection sheaths as Mead originally intended.

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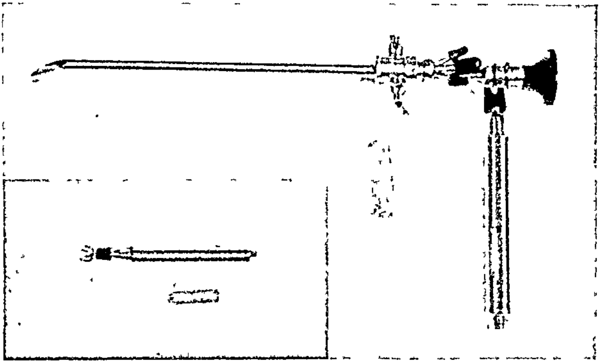
The Journal of Urology
Vol 75, No 6, June 1956
Printed in U S A.

A SIMPLE CYSTOSCOPIC ILLUMINATOR

BEN SEID AND BERNARD E COHLER

The McCarthy illuminator for endoscopic instruments is an ingenious device for providing a light source, at the same time eliminating the annoying cords, electric lines, transformers, rheostat boxes and possibilities of shock; but it has a few drawbacks in preventing full turns of the cystoscope as it impinges on the water-source locks, and is too costly.



The thought occurred to the authors that an illuminator could be made more cheaply and very easily by anyone handy with a soldering iron. The simple directions for making the illuminator follow:

1) Remove the light bulb from an ordinary pocket flashlight,

2) Cut off light connector (co-axial plug) from ordinary cystoscope light cord,

3) Solder light connector end to metal head of flashlight through bulb socket so that a good contact is made with battery terminal,

4) Use flashlight with self-retaining flick switch at base or side, so that the light may be used intermittently or constantly as desired.

The total cost of the device is about $2 at the most. The cost in battery replacement is very slight. The flashlight handle affords a good grip for holding the cystoscope and a full 360 degree turn is easily made in any direction without obstruction. There is no danger of shock because the voltage is 3 volts or less. In those scopes where bulbs take 1.5 volts or less, a dummy battery may be inserted to halve the voltage. This dummy battery is made by hammering a nail lengthwise through a piece of dowel the size of a battery and flattening the point.

The ease of making this low cost device, the lightness in weight, and correction of the objectionable features of the McCarthy box, should make this device a boon and a popular item for cystoscopists and endoscopists.

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SECTION MEETINGS

Mid-Atlantic—Cavalier Hotel, Virginia Beach, Va. March 21–24, 1957
Northeastern—Equinox House, Manchester, Vt. September 9–12, 1956
North Central—Cleveland, Ohio, October 3–5, 1956
South Central—Mexico City, Hotel Del Prado, October 28–31, November 1, 1956
Southeastern—Atlanta, Ga. April 7–11, 1957

Note by editor. A complete list of the executive committees of the various sections, and a complete list of the officers and members of the executive committees of the various branch societies will be printed in the December 1956 issue.

The names of the new officers and members of the Executive Committee of the American Urological Association for 1956–57 will be printed in the July issue.

INDEX

Abeshouse, B S and Tiongson, A T Paraplegia, a rare complication of translumbar aortography, 348
Abramson, A S, see Michael Kenney, jt auth
Acid phosphatase activities of various human tissues, 857
Acid phosphatase determinations, use of L tartrate, 143
ACTH, effect on urinary excretion of androgens and other steroids by old men in comparison with young men, 558
Adrenal, new growths, adenoma, 579
Air embolism during presacral pneumography, 569
Allergy allergic manifestations of 70 per cent urokon, 1011, 1016
Amelar, R D Carcinoma of penis due to trauma occurring in male patient circumcised at birth, 728
American Cystoscope Makers, Inc, Kiefer alteration of McCarthy cystoscope to permit use of Mead telescope, 1025
  Rinker lock splint for intubated ureterotomy, 52
American Urological Association, officers and executive committee, 1955–1956, 1028
  Sections' presidents and secretaries, 1028
Amyloidosis, 122, 424
Anderson, D O, see Hans Marberger, jt auth
Anderson, W L, see B W Young, jt auth
Aneurysm, see Kidney, aneurysm
Angrist, A A, see J B Wallach, jt auth
Antibiotics, see also Cortisone, Drugs, Penicillin, etc
  urinary tract infections, 892
Antrenyl, urinary retention due to, 342
Aorta, excision of occluded abdominal aorta and common iliac arteries and replacement with homograft for urinary incontinence in Leriche syndrome, 961
  graft, excision of occluded abdominal aorta and common iliac arteries and replacement with homograft for treatment of incontinence in Leriche syndrome, 961
Aortography 169, 348, 615, 846, 961
  complications associated with, 846
  diagnosis of renal neoplasms, 615
  paraplegia, complication of, 348
  technique of translumbar aortic catheterization, 169
Apparatus, see Armamentarium
Appendix, incarcerated scrotal appendicitis, 811
Appleton, D M and Waisbren, B A Prophylactic use of chloramphenicol in transurethral resections of prostate gland, 304
Arconti, J S and Goodwin, W E Use of scrotal skin to cover wound defects in groin and pubic area, 292
Armamentarium, Browne basket bougie for extraction of ureteral calculi, 55
  Comarr and Torgerson method of retaining catheters, 1019
  Cuéllar silver trocar for translumbar aortic catheterization, 169
  Forsythe, Steuber and Hamilton aid for maintenance of sterility of drainage tubes, 1023
  Hurwitz and Jacobson new Timberlake obturator for passage of resectoscope under adverse conditions, 878
  Kiefer alteration of McCarthy cystoscope to permit use of Mead telescope, 1025
  Lipton bladder scoop, 877
  Rinker lock splint for intubated ureterotomy, 52
  Seid and Cohler simple cystoscopic illuminator, 1027
  Uhle and Mackinney use of Foley catheter for control of stress incontinence in women, 79
Artery, aneurysm of renal artery, 380
  arteriovenous aneurysm of kidney, 586
  epithelial morphology of autogenous grafts when utilized as ureteral and vesical substitutes in experimental animal, 659
  excision of common iliac arteries and occluded abdominal aorta for treatment of urinary incontinence in Leriche syndrome, 961
Atherton, L D, see Lytle Atherton, jt auth

Atherton, Lytle and Atherton, L. D. Radical retropubic prostatectomy for carcinoma, 111
Austen, George, Jr., see Lester Persky, jt. auth.
Autopsy incidence of uremia, clinical implications, 356
Azoury, B. S., Scardino, P. L. and Prince, C. L. Vesicovaginal fistula, 75

Bacteria, flora of urine specimens from normal adults, 562
Baker, W. J. and Graf, E. C. Experiences with ileal conduit in urinary diversion, 950
Banthine, urinary retention due to, 342
Bard, C. R. Inc., Browne basket bougie for extraction of ureteral calculi, 55
Bard, C. R. Inc., Lipton simplified bladder scoop, 877
Barnes, M. L., see Robert Lich, Jr.
Batal, J. T., see E. J. Ganem, jt. auth.
Baurys, William. Serious complications associated with newer diagnostic methods in urology, 846
Belfield, William R., 1955 Memorial Lecture, 892
Benadryl, intravenous injections, effect in allaying allergic manifestations of intravenous urokon, 1016
Beneventi, F. A. and Marshall, V. F. Some studies of urinary incontinence in men, 273
Benjamin, J. A., Betheil, J. J., Emmel, V. M., Ramsey, G. H. and Watson, J. S. Observations on ureteral obstruction and contractility in man and dog, 25
Berglund, E. B., see T. H. Sweetser, jt. auth.
Bergman, Harry, see S. J. Schneierson, jt. auth.
Beta-naphthylamine-induced dog bladder papillary transitional tumors, 690
Betheil, J. J., see J. A. Benjamin, jt. auth.
Biochemistry studies, 95, 470, 772, 824, 950
Biopsy, simplified scoop for retrieving from bladder, 877
Bischoff, A. J. and Fishkin, B. G. Carcinoma of urinary bladder with cutaneous metastasis, report of 4 cases, 701
Bladder, amyloidosis, 122
  artificial, see Bladder, substitute
  atonic, neurogenic, 465
  biopsy, simplified scoop for retrieving, 877
  calculi, application of ultrasonic energy to, 865
    simplified scoop for retrieving, 877
  comparative study of effect of various anticholinergic drugs on bladder stimulated by furmethide, 665
  contracture, associated with urinary schistosomiasis, 671
    of neck associated with true ureteral prolapse and meatal stenosis, 223
  cystectomy for hypotonic bladder, 456
  cystitis cystica, 443
    emphysematosa, 256
    interstitial, see Bladder, interstitial cystitis
  cystography in children, 151
  cysts, dermoid, 801
  dermoid cysts, 801
  dysfunction, neurogenic, 456
    neurogenic, ileal loop diversion of urine, 470
  epispadias, 173
  epithelial morphology of autogenous grafts when utilized as ureteral and vesical substitutes, 659
  exstrophy, 173
    plastic surgery, 448
  fistula, vesicovaginal, 75
  hypertonia, 456
  incontinence in Leriche syndrome, 961
    postoperative, 273
  injury, during pelvic surgery and radiation on female, 433
  interstitial cystitis, intramural injection of hydrocortone hyaluronidase for, 63
    management by differential sacral neurotomy, 261
  irrigations, hypothermia induced by, 1006
  lesions associated with spina bifida, 537
  neurogenic dysfunction, 456, 465
  new growths, adenocarcinoma, 1012
    amyloid, 687
    carcinoma, classification when associated with schistosomiasis and metaplasia, 680
    carcinoma, cutaneous metastasis from, 697, 701
    homotransplantation to intact vesical epithelium, 690
    initial carcinoma, survival rates in relation to therapy, 480, 492
    modified position for transurethral resection in women, 73
    recurrence by surgical implantation, 695
    secondary malignant tumors metastatic

    from primary foci in distant organs, 965
  paralysis, complication of aortography, 348
    retrograde urinary infection along indwelling catheter drainage system, 737
    10 year followup of World War II paraplegic, 66
  plastic surgery for exstrophy, 448
  radon implantation for carcinoma, 492
  schistosomiasis, classification of carcinoma associated with, 680
  scoop, 877
  segmental resection for carcinoma, 492
    to control hematuria due to metastatic adenocarcinoma from breast, 965
  substitute, 470, 659, 950
  tuberculous ulcers, clorpactin for, 375
  urinary retention due to drugs, 342
Bladder neck, contracture, 173
  associated with true ureteral prolapse and meatal stenosis, 223
Blood chemistry changes following transurethral prostatic resection, 95
Blood chemistry studies in patients undergoing transurethral prostatic resection, 824
Blood, detection in urine, simple test, 743
  hematuria, significance in young men, 135
  uremia, autopsy incidence, 356
Bobeck, C J, see W C Wikner, jt auth
Body section radiography, 615
Bone formation in ureter, 793
Bone, sarcoma metastasizing to kidney, 21
Bonte, F J, see Lester Persky, jt auth
Boren, J S see R H Harrison III, jt auth
Boren, J S, see N S R Maluf, jt auth
Boyd, R E, see Jack Lapides, jt auth
Braman, Robert and Cross, R R Jr Perinephric abscess producing a pneumonephrogram, 194
Brandes, G E, see N S R Maluf, jt auth
Brown, A W, see A L Miller, Jr
Browne, H S Improved basket bougie for extraction of ureteral calculi, 55
Bulkley, G J Modified catheter for drainage of cutaneous ureterostomy, 875
Bulkley G J, Cooper, J A D and O'Conor, V J Present status of treatment of carcinoma of prostate with radioactive materials 837
Bunts, R C, see K H Lord, jt auth
Burke, D E, see J J Kaufman, jt auth
Burns, Edgar and Peiser, Irving Treatment of urologic complications in gynecology, 438
Butcher, H R Jr and Sleator, William, Jr Effect of ureteral anastomosis upon conduction of peristaltic waves, electro ureterographic study, 650

Calculi, see various organs, also Urinary tract
Campbell, J H, see E C St Martin, jt auth
Campbell, Meredith Resection of solitary kidney, 900
Cancer, see various organs and regions
Candidiasis, fatal, disseminated, following routine use of penicillin and streptomycin, 930
Carcinoma, see various organs and regions
Cardiovascular system, circulatory collapse in infants following cystoscopy, 1016
Catheter, balloon, use for control of stress incontinence in women, 79
  drainage system, retrograde infection along, in paraplegia, 737
  for drainage of cutaneous ureterostomy, 875
  plugs, aid for maintenance of sterility, 1023
  simple method of retaining, 1019
  splinting, for intubated ureterotomy, 52
Cauble, W G see A M Tocker, jt auth
Cauffield, E W Dermoid cysts of bladder, 801
Cecil, A B Radical operation for cure of intractable stricture of male urethra, 501
Cerebrospinal fluid pressure during transurethral prostatic resection, 824
Chait, Alejandro Renal functional pattern in calculous disease 937
Chalek, C C, see J H Woodruff, Jr, jt auth
Chapman, W H, see C W Vermeulen, jt auth
Chisholm, T C, see T H Sweetser, jt auth
Chloramphenicol, prophylactic use in transurethral prostatic resection, 304
Chloride concentration changes during transurethral prostatic resection, 824
Chromic phosphate therapy for prostatic carcinoma, 837

Chute, Richard and Ireland, E. F. Jr. Dependent drainage via perineum in retropubic prostatectomy, 530
Cian, L. G., see H. J. Davis, jt. auth.
Citrate excretion, effect of diet on, 216
Clapper, W. E. and Plank, L. E. Clinical response of urinary tract infections treated by elkosin, gantrisin, triple sulfa or triple sulfa-achromycin, 339
Clarke, B. G., Goade, W. J. Jr., Rudy, H. L. and Rockwood, Lawrence. Differential diagnosis between cancer and solitary serous cyst of kidney, 922
Clarke, B. G., Hurwitz, I. S. and Dubinsky, Eli. Solitary serous cysts of kidney, biochemical, cytological and histologic studies, 772
Clausen, Hans. Clearance speed, a new clearance method, 361
Clausen, Hans. Clearance without prolonged infusion, with only one clearance period, a new clearance formula, and without a catheter, 364
Clearance method tests, 361, 364
Coats, E. C. Application of ultrasonic energy to urinary and biliary calculi, 865
Cobalt 60, 881
Cohler, B. E., see Ben Seid, jt. auth.
Coleman, F. P., see Saul Kay, jt. auth.
Collins, W. T., see W. P. Mulvaney, jt. auth.
Colon, J. E., see R. A. Marcial-Rojas, jt. auth.
Comarr, A. E. and Torgerson, T. Simple method of retaining catheters, 1019
Cooper, Dean, see G. S. Rost, jt. auth.
Cooper, J. A. D., see G. J. Bulkley, jt. auth.
Corey, E. L., Fite, E. H. Jr. and Vest, S. A. Electropotential changes in normal human ureter, 244
Cortisone, effect on spermatogenic function of testis, 527
  treatment for epididymitis, 133
Creevy, C. D. Partial cystectomy for hypotonic bladder, report of 11 cases, 456
Crenshaw, W. B., see R. M. Nesbit, jt. auth.
Cross, R. R. Jr., see Robert Braman, jt. auth.
Cuéllar, Jorge. New technique of translumbar aortic catheterization, 169
Curtiss, Charlotte and Hock, Ernest. Intrascrotal adenomatoid tumor, case report, 292
Cystoscope, illuminator, 1027
  sterilization, 375
Cystoscopy, hypothermia induced by, 1006
Cytology, diagnosis of kidney cancer, 551
  screening method in prostatic carcinoma, 734
  studies of solitary serous cysts, 772

Davis, H. J. and Cian, L. G. Positive pressure urethrography, new diagnostic method, 753
Davis, J. B., Whitaker, J. D., Ding, L. K. and Kiefer, J. H. Disseminated, fatal, postpartum candidiasis with renal suppuration, case report, 930
Davol Rubber Co., Davis and Cian catheter for injection of contrast medium, 753
Dean, A. L. Carcinoma of male and female urethra, pathology and diagnosis, 505
Deaver, G. G., see P. A. Morales, jt. auth.
Dees, J. E. Prognosis of primary tumors of renal pelvis and ureter, 419
Dehydration, effect on formation of kidney calculi, 209
Delagi, E. F., see Michael Kenney, jt. auth.
Demerol, urinary retention due to, 342
Devine, K. D., see D. C. Wormer, jt. auth.
DeWeerd, J. H. and Simon, H. B. Simple renal cysts in children, review of literature and report of 5 cases, 912
Diet, influence on urinary citrate excretion, 216
Dimmette, R. M., Sproat, H. F. and Sayegh, E. S. Classification of carcinoma of urinary bladder associated with schistosomiasis and metaplasia, 680
Dimmette, R. M., see E. S. Sayegh, jt. auth.
Ding, L. K., see J. B. Davis, jt. auth.
Dog, clinical implications of transplantability of induced bladder tumors to intact transitional epithelium, 690
  effect of ureteral anastomosis upon conduction of peristaltic waves, electroureterographic study, 650
  epithelial morphology of autogenous grafts when utilized as ureteral and vesical substitutes, 659
  hypothermia induced by cystoscopy, 1006

  lipids in prostate gland, 324
  route of backflow in acute hydronephrosis established by radioautographs, 190
  ureteral obstruction and contractility, 25
  ureteral regeneration following segmental resection, 796
    without intubation, 43
D'Oranzio, G B, see Michael Kenney, jt auth
Drainage of bladder following retropubic prostatectomy by way of perineum, 530
Drainage system, retrograde urinary infection along indwelling catheter in paraplegia, 737
Drainage tubes, aid for maintenance of sterility, 1023
Draper, J W and Sierp, Mieczyslaw Comparative study of effect of various anticholingeric drugs on human bladder which had been stimulated by furmethide, 665
Drugs, see also specific names
  anticholinergic, comparative study of effect on bladder stimulated by furmethide, 665
  urinary retention due to, 342
Dubinsky, Eh, see B G Clarke, jt auth

Edwards, J G Intrinsic renal function, 200
Eikner, W C and Bobeck, C J Renal vein thrombosis, 780
Electromyogram, ureteral, 244
Electron microscopy of cystine urolith, 940
Electroureterography, 650
Electrourogram, 250
Elkosin, urinary tract infections, 339
Embolism, air, during presacral pneumography, 569
Emmel, V M, see J A Benjamin, jt auth
Emmett, J L, see D C Wormer, jt auth
Endocrine therapy, cryptorchidism, 973
  effect of ACTH administration on urinary excretion of androgens and other steroids by old men in comparison with young men, 558
  infertility, 852
Enzyme, prostatic, and abnormal bleeding, 116
Ephedrine, urinary retention due to, 342
Epididymis, epididymitis, treatment by cortisone, 133
  new growths, bilateral adenomatoid tumor, 819
Ethinyl estradiol therapy for infertility, 852
Feo, L G, Fetter, T R, Peoples, D M and Morton, H E Bacteria associated with trichomonas vaginalis in male urethritis, 711
Ferguson, Paul, see G S Rost, jt auth
Fetter, T R and Warren, K C Congenital urinary tract obstructions in children, 173
Fetter, T R, see L G Feo, jt auth
Figueroa, J J, see R A Marcial Rojas, jt auth
Fishkin, B G, see A J Bischoff, jt auth
Fishman and Lerner technique for determining L tartrate inhibited prostatic acid phosphatase, 143
Fistula, renocolic, 787
  vesicovaginal 75
Fite, E H Jr, see E L Corey, jt auth
Flocks, R H Treatment of urethral tumors, 514
Florence T J Cortisone in treatment of epididymitis, 133
Foley catheter, use for control of stress incontinence in women, 79
Forsythe, W E, Stueber, P J Jr and Hamilton, M H An aid for maintenance of sterility of drainage tubes, 1023
Fowler, V B, see J T MacLean, jt auth
Francke, Paul, see J W Lane, jt auth
Free, A H, see H M Free, jt auth
Free H M, Free, A H and Giordano, A S with technical assistance of C M Ziems Studies with a simple test for detection of occult blood in urine, 743
Furmethide comparative study of effect of various anticholinergic drugs on human bladder stimulated by, 665

Gallbladder, calculi, application of ultrasonic energy to, 865
Ganem, E J and Batal, J T Secondary malignant tumors of bladder, 965
Gangrene, Fournier's gangrene of penis and scrotum, 719
Gantrisin urinary tract infections, 339
Gardner, J S Plastic repair of hydronephrosis, description of new technique used in 10 cases, 367
Gartman, Edward Intraurethral verruca acuminata in men, 717
Gartman, Edward Significance of hematuria in young men 135
Gas forming infections in urinary tract 194

Genital tract, amyloidosis, 122
  sclerosing lipogranuloma of testicle, 334
Gerende, J. H., see F. K. Mostofi, jt. auth.
Gibson, T. E. Hydronephrosis, 1
Giordano, A. S., see H. M. Free, jt. auth.
Glans penis, see Penis
Glass, Macellis, see J. B. Wallach, jt. auth.
Glassman, Irving, Shapiro, Robert and Robinson, Franklin. Air embolism during presacral pneumography, case report, 569
Goade, W. J. Jr., see B. G. Clarke, jt. auth.
Gold 198, 881
Goldstein, A. E. and Heller, Eugene. Ectopic ureter opening into seminal vesicle, 57
Goodwin, W. E., see J. S. Arconti, jt. auth.
Goodwin W. E., see J. J. Kaufman, jt. auth.
Gordon, Wilfred. Nonhormonal adrenal adenoma, report of 2 cases, 579
Graf, E. C., see W. J. Baker, jt. auth.
Grafts, fascia lata, 659
Greenfield, Michael. True prolapse of ureter, case report and review of literature, 223
Greenwald Co., Lipton simplified bladder scoop, 877
  Hurwitz and Jacobson new Timberlake obturator attachment for passage of resectoscope under adverse conditions, 878

Hamilton, M. H., see W. E. Forsythe, jt. auth.
Hamm, F. C. and Weinberg, S. R. Experimental studies of regeneration of ureter without intubation, 43
Hancock, R. A. Modified position for transurethral resection of bladder tumors in women, 73
Hand, J. R. Undescended testes, 973
Harrison, J. H., see D. A. MacFarlane, jt. auth.
Harrison, R. H. III, Boren, J. S. and Robison, J. R. Dilutional hyponatremic shock: Another concept of transurethral prostatic resection reaction, 95
Hartz, P. H. and Santander, Ernesto. Amyloid tumor of bladder, 687
Heckel, N. J., see J. H. McDonald, jt. auth.
Heller, Eugene, see A. E. Goldstein, jt. auth.
Herman, J. R. Incarcerated scrotal appendicitis, 811
Herrold, R. D. The story of antimicrobial agents for urinary infections and some new concepts, 892
Higbee, D. R. and Millett, W. D. Localized amyloidosis of ureter, case report, 424
Hinman, Frank, Jr. Recurrence of bladder tumors by surgical implantation, 695
Hinman, Frank Jr. and Oppenheimer, Rudolf. Smooth muscle regeneration in repair of experimental ureteral defects, the significance of double lumen, 428
Histology, studies of solitary serous cysts, 772
Hock, Ernest, see Charlotte Curtiss, jt. auth.
Hotchkiss, R. S., see P. A. Morales, jt. auth.
Hudson, H. C. Osteogenic sarcoma involving left kidney, 21
Huffman, W. L., McCorkle, H. F. and Persky, Lester. Unilateral regeneration following experimental segmental resection, 796
Hurwitz, I. S., see B. G. Clarke, jt. auth.
Hurwitz, S. P. and Jacobson, E. C. New Timberlake obturator attachment for passage of resectoscope under adverse conditions, 878
Hydrocortone hyaluronidase, intramural injection for interstitial cystitis, 63
Hydrostatic pressure of irrigation fluid during transurethral prostatic resection, 824
Hyman, R. M., see J. M. Silberblatt, jt. auth.
Hypothermia induced by cystoscopy, 1006

Ileum, loop for urinary diversion in neurogenic bladder dysfunction, 470
  use of isolated segment for substitute bladder, 950
Infertility, see Sterility
Inguinal region, condyloma acuminatum, 292
  use of scrotal skin to cover wound defects, 292
Instruments, see Armamentarium
Inulin, clearance and plasma extraction ration of, for measurement of renal plasma flow, 200
Ireland, E. F. Jr., see Richard Chute, jt. auth.
Irradiation, see Radiation
Irrigation fluids, effect on patients under-

    - going transurethral prostatic resection, 824
- Isoniazid combined with streptomycin and sodium PAS for renal tuberculosis, 375
- Isotopes, 881

- Jacobson, E B, see S P Hurwitz, jt auth
- Jaffar, D J, Sewell, G R and Schwarz, F W Johanson urethroplasty for repair of urethral strictures, 805
- Johanson urethroplasty for repair of urethral strictures, 805

- Kaufman, J J, Burke, D E and Goodwin, W E Abdominal venography in urological diagnosis, 160
- Kay, Saul and Coleman, F P Duplication of left undescended testicle, case report, 815
- Kearns, W M Treatment of male infertility with estrogenic substance 852
- Kenney, Michael, Weiss, A A, Lindenauer, H J, Delagi, E F, D'Orazio, G B and Abramson, A S Retrograde urinary infection along indwelling catheter drainage system in paraplegia, 737
- Kidney, abscess, perinephric, producing pneumonephrogram, 194
  - aneurysm of renal artery 380
  - arteriovenous aneurysm, 586
  - artery, bifurcation, 229
  - calculi, application of ultrasonic energy to, 865
    - effect of temperature, humidity and dehydration on formation 209
    - electron microscopy, 940
    - experimental, state of calcium in urine, 592, 602
    - function pattern in 937
    - in mink, pathology, bacteriology and experimental production, 602
  - calyces, pyelectasis, 12
  - colic due to ureterolithiasis, 209
  - cyst, solitary carcinoma within 627
    - solitary, differential diagnosis between cancer and 922
  - cysts confined to pyramids, 776
    - in children, 912
    - percutaneous puncture, diagnosis of neoplasms 615
  - diagnosis of tumors by abdominal venography 160
  - fistula renocolic, acquired, 787
  - function, 200
    - pattern in calculous disease, 937
    - test, 361, 364
  - fusion 17
  - heminephrectomy, 173
  - hydronephrosis 1, 173, 190, 242
    - intermittent importance of pyelography during episodes of pain, 767
    - plastic repair, 367
  - infarcts, 780
  - insufficiency autopsy incidence of uremia, 356
  - left, low lying position, 198
  - lesions associated with spina bifida, 537
  - leukoplakia of pelvis, 633
  - metastases from osteogenic sarcoma 21
  - nephrogram, 615
    - produced by perinephric abscess 194
  - nephrography during routine excretory urography 572
  - nephrostomy catheters, method of retaining 1019
  - new growths, carcinoma within solitary cyst, 627
    - diagnosis by cytology, false positives, 551
      - by urography, 615
    - differential diagnosis between solitary serous cyst and, 922
    - hypernephroma, diagnosis by abdominal venography, 160
    - of pelvis and ureter, diagnosis 416
    - of pelvis, pathology, 384
      - prognosis, 419
    - Wilms' tumor, diagnosis by abdominal venography, 160
  - obstruction see also Kidney hydronephrosis
    - ureteropelvic, 1, 173
  - operation for simple cyst in children 912
  - perinephric abscess producing pneumonephrogram, 194
  - plasma flow as measured by clearance and plasma extraction ratio of inulin, 200
  - plastic operation for hydronephrosis, 367
  - pneumonephrogram produced by perinephric abscess, 194
  - pyelectasis, 12
  - pyelostomy catheters, method of retaining, 1019
  - reflux in acute hydronephrosis, 190
  - resection of solitary organ, 900
  - solitary cyst, carcinoma in, 627
  - solitary, resection, 900

solitary serous cysts, biochemical, cytologic and histologic studies, 772
tuberculosis, status of chemotherapy, 375
ureteropelvic obstruction, 1
urography, antegrade, 615
vein thrombosis, 780
Kidney pelvis, leukoplakia, 633
new growths, diagnosis, 416
pathology, 384
prognosis, 419
pyelectasis, 12
Kiefer, J. H. Alteration of McCarthy cystoscope to permit use of Mead telescope, 1025
Kiefer, J. H., see J. B. Davis, jt. auth.
Kiefer, J. H., see M. D. Slominski-Laws, jt. auth.
King, G. G., see B. W. Young, jt. auth.
Klein, E. I., see M. J. Williams, jt. auth.
Klinger, M. E. Bone formation in ureter, 793
Kneucker, A. W. The electrourogram. II. Experimental study, 250
Knouf, C. E., see G. S. Rost, jt. auth.

Lane, J. W. and Francke, Paul. Cystitis emphysematosa, case report, 256
Lapides, Jack and Boyd, R. E. Effect of intravenous benadryl in allaying allergic manifestations of 70 per cent urokon, 1016
Lattimer, J. K. and Spirito, A. L. Current status of chemotherapy of renal tuberculosis, 375
Leadbetter, W. F. and Shaffer, F. G. Ileal loop diversion, its application to treatment of neurogenic bladder dysfunction, 470
Leman, C. B., see D. A. MacFarlane, jt. auth.
Leriche syndrome, urinary incontinence in, 961
Levitin, M. S., see F. K. Mostofi, jt. auth.
Lewis, E. L. and Cletsoway, R. W. Megaloureter, 643
Lich, Robert, Jr., Mauer, J. E. and Barnes, M. L. Pyelectasis, 12
Lich, Robert, Jr., see J. J. Robbins, jt. auth.
Lindenauer, H. J., see Michael Kenney, jt. auth.
Lipton, J. H. Simplified bladder scoop, 877
Lisa, J. R., see Heino Provet, jt. auth.
Lord, K. H. and Bunts, R. C. Present urologic status of World War II paraplegic, 10-year followup, 66
L-tartrate, use in determining prostatic serum acid phosphatase, 143

MacFarlane, D. A., Leman, C. B., Munson, P. L. and Harrison, J. H. Effect of ACTH administration on urinary excretion of androgens and other steroids by old men in comparison with young men, preliminary report, 558
Mackinney, C. C., see C. A. W. Uhle, jt. auth.
MacLean, J. T. and Fowler, V. B. Pathology of tumors of renal pelvis and ureter, 384
Malek, L. H., see Hans Marberger, jt. auth.
Maluf, N. S. R. Method for relief of upper ureteral obstruction within bifurcation of renal artery, 229
Maluf, N. S. R., Boren, J. S. and Brandes, G. E. Absorption of irrigating solution and associated changes upon transurethral electroresection of prostate, 824
Marberger, Hans, Riedesel, R. D., Anderson, D. O. and Malek, L. H. Comparative study of phosphatase activities of various human tissues, 857
Marcial-Rojas, R. A., Colon, J. E. and Figueroa, J. J. Sclerosing lipogranulomas of male genitalia, report of one case and review of literature, 334
Marshall, V. F., see F. A. Beneventi, jt. auth.
Martin, W. J., see D. C. Wormer, jt. auth.
Mathes, Gordon, Richmond, S. G. and Sprunt, D. H. Use of L-tartrate in determining "prostatic" serum acid phosphatase: Report of 514 cases, 143
Maurer, J. E., see Robert Lich, Jr., jt. auth.
McCarthy cystoscope, Kiefer's alteration to permit use of Mead telescope, 1025
McClellan, R. E. A low lying left kidney, 198
McCorkle, H. F., see W. L. Huffman, jt. auth.
McCrary, Ashton, see G. S. Rost. jt. auth.
McDonald, D. F. and Thorson, Theodore. Clinical implications of transplantability of induced bladder tumors to intact transitional epithelium in dogs, 690

McDonald, J H and Heckel, N J Effect of cortisone on spermatogenic function of human testes, 527

McDonald, J H and Heckel, N J Further observations on rebound phenomenon in treatment of certain types of spermatogenic dysfunction, 990

McDonald, J H and Heckel, N J Primary amyloidosis of lower genitourinary tract, 122

Mead telescope, use in Kiefer's alteration of McCarthy cystoscope, 1025

Meirowsky, A M, see M K Moulder, jt auth

Metabolism, atonic, neurogenic bladder in porphyria, 465

Miller, A L, Jr, Brown, A W and Tomskey, G C Pelvic fused kidney, 17

Miller, G H, see C W Vermeulen, jt auth

Millett, W D, see D R Higbee, jt auth

Mink, urolithiasis pathology, bacteriology and experimental production, 602

Miokon, new intravenous urographic medium, 758

Montgomery, P O'B, see W M Nickey jt auth

Moos, W S Basic aspects of radiation therapy, 881

Morales, P A, Deaver, G G and Hotchkiss, R S Urological complications of spina bifida in children 537

Morin L J Bilateral adenomatoid tumor of epididymis, 819

Morton, H L, see L G Feo, jt auth

Mostofi F K, with statistical assistance of M S Levitin and J H Gerende Study of 2678 patients with initial carcinoma of bladder I Survival rates, 480

Mostofi, F K, with statistical assistance of M S Levitin and J H Gerende Study of 2678 patients with initial carcinoma of bladder II Survival rates in relation to therapy, 492

Moulder, M K and Meirowsky A M Management of Hunner's ulcer by differential sacral neurotomy, preliminary report, 261

Mulvaney, W P and Collins, W T Cystic disease of renal pyramids, 776

Munson, P L, see D A MacFarlane, jt auth

Muscle regeneration of ureter following segmental resection, 796

Musculoskeletal system, bone formation in ureter, 793
  bone sarcoma metastasizing to kidney, 21
  distribution of bone lesions in kidney neoplasms, 615

Nervous system, differential sacral neurotomy for interstitial cystitis 261
  retrograde urinary infection along indwelling catheter drainage system in paraplegia, 737
  status of World War II paraplegic, 66

Nesbit R M Diagnosis of intermittent hydronephrosis Importance of pyelography during episodes of pain 767

Nesbit, R M Is cystitis cystica an innocent or malefic lesion, 443

Nesbit, R M and Crenshaw, W B Aneurysm of renal artery, 380

Nickey, W M and Montgomery, P O'B Eosinophilic granulomatous prostatitis, 730

Nicolai C H Miokon, new intravenous urographic medium, 758

Nielsen I M Urolithiasis in mink, pathology bacteriology and experimental production, 602

Occultest use in test for detection of blood in urine, 743

O'Conor V J Diagnosis of tumors of renal pelvis and ureter, 416

O Conor, V J, see G J Bulkley, jt auth

Operations, see various organs and regions, also specific names of operations under various organs and regions

Oppenheimer, Rudolf, see Frank Hinman, Jr, jt auth

Oravisto, K J and Schauman, S Urethrocystography in differential diagnosis of prostatic cancer, 995

Orthotolidin, use in test for detection of blood in urine, 743

Ottoman, R E, see J H Woodruff, jt auth

Papanicolaou technique as screening method in prostatic carcinoma, 731
  for examination of urine in diagnosis of kidney cancer, false positives, 551

Para aminohippurate, determination of renal plasma flow by excretion of, 200

Para aminohippuric acid, use in determination of clearance speed, 361, 364

Para amino salicylic acid combined with

streptomycin and isoniazid for renal tuberculosis, 375

Paralysis, 66, 348, 737

Pathology, carcinoma of bladder, 480
  of kidney pelvis, 384
  of urethra, 505

Peiser, Irving, see Edgar Burns, jt. auth.

Penicillin, see also Antibiotics; Urinary Tract, infections
  fatal disseminated candidiasis following routine use after cesarean section, 930

Penis, circumcision at birth, carcinoma due to trauma, 728
  Fournier's gangrene, 719
  new growths, carcinoma due to trauma occurring in patient circumcised at birth, 728
    carcinoma, recurrent pubic skin lesions, 292

Peoples, D. M., see L. G. Feo, jt. auth.

Perineum, dependent drainage by way of, in retropubic prostatectomy, 530

Peristalsis, effect of ureteral anastomosis upon, electro-ureterographic study, 650

Persky, Lester, Bonte, F. J. and Austen, George, Jr. Mechanisms of hydronephrosis: Radioautographic backflow patterns, 190

Persky, Lester, see W. L. Huffman, jt. auth.

Pesquier, C. M., see E. C. St. Martin, jt. auth.

Petkovic, S. D. Clinical study of urethral injuries, 81

Phenolsulfonphthalein, determination of renal plasma flow by excretion of, 200

Philpot, V. B. Jr. Bacterial flora of urine specimens from normal adults, 562

Phosphatase activities of various human tissues, 857

Physiology, effect of ureteral anastomosis upon conduction of peristaltic waves, electro-ureterographic study, 650

Plank, L. E., see W. E. Clapper, jt. auth.

Pneumography, air embolism during, 569
  retroperitoneal, complications, 846

Pneumonephrogram produced by perinephric abscess, 194

Politano, V. A. Leukoplakia of renal pelvis and ureter, 633

Presti, J. C., see H. M. Weyruach, jt. auth.

Prince, C. L., Scardino, P. L. and Wolan, C. T. Effect of temperature, humidity and dehydration on formation of renal calculi, 209

Prince, C. L., see B. S. Azoury, j. auth.

Prostate, acid phosphatase activity, 857
  amyloidosis, 122
  enzymes, and abnormal bleeding following orchiectomy for metastatic prostatic carcinoma, 116
  lipids in dog, 324
  new growths, carcinoma, abnormal bleeding following orchiectomy due to circulating proteolytic enzyme, 116
    carcinoma complicated by epidermoid carcinoma of urethra, 314
      cytology as screening method, 734
      treated by radioactive materials, 837
      urethrocystography in differential diagnosis, 995
    operations, statistics, 1000
    radical perineal prostatectomy, 1000
    use of L-tartrate in determining serum acid phosphatase, 143
  operations for carcinoma, statistics, 1000
  prostatectomy, incontinence following, 273
    perineal, radical, 1000
    retropubic, dependent drainage by way of perineum, 530
  prostatitis, eosinophilic, granulomatous, 730
  transurethral resection, see also Resection, Resectoscope
    absorption of irrigating solution and associated changes, 824
    prophylactic use of chloramphenicol, 304
    reaction following, characterized by dilutional hyponatremic shock, 95
    statistics in carcinoma, 1000

Protein concentration changes during transurethral prostatic resection, 824

Provet, Heino, Lisa, J. R. and Trinidad, Salvatore. Tubular carcinoma of kidney within solitary cyst, 627

Radiation therapy, basic aspects, 881
  pelvic carcinoma, injury of bladder and ureter, 433

Radioactive gold therapy, 837, 881

Radioautographs, use in establishing route of backflow in acute hydronephrosis, 190

Radiography, see also Urography

Radiography, body section, 615

Radioisotopes, 881

Radon implantation for bladder carcinoma, 492

Ramsey, G. H., see J. A. Benjamin, jt. auth.

- Rats, artificial insemination with testicular tissue, 993
- Redeker, A G Atonic neurogenic bladder in porphyria, 465
- Resection, transurethral, for bladder neck contracture, 173
  - of bladder tumors in women, 73
- Resectoscope, new Timberlake obturator attachment for passage of instrument, 878
- Retroperitoneal pneumography, complications, 846
- Reynolds, L R , see T L Schulte, jt auth
- Richmond, S G , see Gordon Mathes, jt auth
- Riedesel, R D , see Hans Marberger, jt auth
- Rinker, J R Use of a lock splint in intubated ureterotomy, 52
- Robbins, J J and Lich, Robert, Jr Metastatic carcinoma of ureter, 242
- Robinson, Franklin, see Irving Glassman, jt auth
- Robison, J R , see R H Harrison III, jt auth
- Rockwood, Lawrence, see B G Clarke, jt auth
- Roentgenography, see Radiography, Urography
- Roland, S I Hypothermia induced by cystoscopy, 1006
- Rost, G S , Cooper, Dean, Knouf, C E Ferguson, Paul and McCrary, Ashton Acquired renocolic fistula in remaining functioning kidney with recovery, case report, 787
- Rudy, H L , see B G Clarke, jt auth
- Rusche, Carl Diagnosis of urologic complications in gynecology, 433

- St Martin, E C , Campbell, J H and Pesquier, C M Cystography in children, 151
- Sanders, A R and Schein, C J Epithelial morphology of autogenous grafts when utilized as ureteral and vesical substitutes in experimental animal, 659
- Santander, Ernesto, see P H Hartz, jt auth
- Sayegh, E S and Dimmette, R M Fibrotic, contracted urinary bladder associated with schistosomiasis and chronic ulceration, a clinicopathological study including treatment, 671
- Sayegh, E S , see R M Dimmette, jt auth
- Scardino, P L , see B S Azoury, jt auth
- Scardino, P L , see C L Prince, jt auth
- Schauman, S , see K J Oravisto, jt auth
- Schein, C J , see A R Sanders, jt auth
- Schistosomiasis complicated by contracted bladder, 671
- Schmidt, S S Anastomosis of vas deferens, experimental study, 200
- Schneierson, S J and Bergman, Harry Acute urinary retention due to drugs, 342
- Schulte T L and Reynolds, L R Transurethral intramural injection of hydrocortone hyaluronidase for interstitial cystitis (Hunner's ulcers), 63
- Schwarz, F W , see D J Jaffar, jt auth
- Scott, E Van Z Prostatic enzymes and abnormal bleeding, 116
- Scrotum, Fournier's gangrene, 719
  - incarcerated appendicitis in, 811
  - new growths, adenomatoid tumor, 297
  - use of skin to cover wound defects in groin and pubic area, 292
- Seaman, A R Lipids in prostate gland of dog, 324
- Seid, Ben and Cohler, B E A simple cystoscopic illuminator, 1027
- Semen, artificial insemination with testicular tissue, 993
  - effect of cortisone on spermatogenic function of human testes, 527
  - oligospermia, testosterone propionate therapy, 990
- Seminal vesicle, ectopic ureter opening into, 57
  - amyloidosis, 122
- Serum chloride changes in patients undergoing transurethral prostatic resection, 824
  - protein and hematocrit changes in patients undergoing transurethral prostatic resection, 824
  - sodium changes in patients undergoing transurethral prostatic resection, 824
- Sewell, G R , see D J Jaffar, jt auth
- Shaffer, F G , see W F Leadbetter, jt auth
- Shapiro, Robert, see Irving Glassman, jt auth
- Sierp, Mieczyslaw, see J W Draper, jt auth
- Silberblatt, J M , Solomon, Cyril and Hyman, R M Exfoliative cytology as

screening method in prostatic carcinoma, 734
Simon, H. B., see J. H. DeWeerd, jt. auth.
Skin, cutaneous ureterostomy, modified catheter for drainage, 875
  metastasis from bladder carcinoma, 697, 701
Slater, G. S. Artificial insemination with testicular tissue, experimental study, 993
Sleator, William, Jr., see H. R. Butcher, Jr., jt. auth.
Slominski-Laws, M. D., Kiefer, J. H. and Vermeulen, C. W. Arteriovenous aneurysm of kidney, case report, 586
Smith, B. A., see E. A. Webb, jt. auth.
Sohval, A. R. Testicular dysgenesis in relation to neoplasm of testicle, 285
Solomon, Cyril, see J. H. Silberblatt, jt. auth.
Spina bifida, complications in children, 537
Spinal cord paralysis following aortography, 348
Spirito, A. L., see J. K. Lattimer, jt. auth.
Sproat, H. F., see R. M. Dimmette, jt. auth.
Sprunt, D. H., see Gordon Mathes, jt. auth.
Sterility and infertility, anastomosis of vas deferens, 300
  artificial insemination with testicular tissue, 993
  observations on rebound phenomenon in treatment of spermatogenic dysfunction, 990
  treatment with estrogenic substance, 852
Sterility of drainage tubes, aid for maintenance, 1023
Streptomycin, see also Antibiotics
  fatal, disseminated candidiasis following routine use after cesarean section, 930
Streptomycin-isoniazid-sodium PAS therapy for renal tuberculosis, 375
Stueber, P. J., Jr., see W. E. Forsythe, jt. auth.
Sulfa-achromycin (triple) urinary tract infections, 339
Sulfa (triple), urinary tract infections, 339
Sweetser, T. H., Chisholm, T. C., Thompson, W. H., Berglund, E. B., Wesolowski, S. P., and Sweetser, T. H., Jr. Exstrophy of urinary bladder: Its treatment by plastic surgery, 448
Sweetser, T. H., Jr., see T. H. Sweetser, jt. auth.
Temperature, effect on formation of kidney calculi, 209
Testis, cryptorchid, 973
    duplication, 815
    endocrine therapy, 973
  new growths, diagnosis by abdominal venography, 160
    relation to testicular dysgenesis, 285
  orchiopexy, 973
  polyorchidism, 815
  sclerosing lipogranuloma, 334
  spermatogenic function, effect of cortisone, 527
  tissue, artificial insemination with, 993
  undescended, 973
    duplication, 815
Testosterone propionate therapy for oligospermia, 990
Thomas, J. F. Fournier's gangrene of penis and scrotum, 719
Thompson, W. H., see T. H. Sweetser, jt. auth.
Thorson, Theodore, see D. F. McDonald, jt. auth.
Tiongson, A. T., see B. S. Abeshouse, jt. auth.
Tocker, A. M. and Cauble, W. G. Urinary incontinence in Leriche syndrome: Treatment by excision of occluded abdominal aorta and common iliac arteries and replacement with homograft, 961
Tomskey, G. C., see A. L. Miller, Jr., jt. auth.
Torgerson, T., see A. E. Comarr, jt. auth.
Trinidad, Salvatore, see Heino Provet, jt. auth.
Triple sulfa, urinary tract infections, 339
Tuberculosis, see various organs and regions
Tuggle, Allan, see V. H. Youngblood, jt. auth.

Uhle, C. A. W. and Mackinney, C. C. Use of vaginal balloon catheter for control of stress incontinence in women, 79
Ultrasonic energy, application to urinary and biliary calculi, 865
Umbradil, use for urethrography and detection of urethral diverticula in female, 753
Uremia, atuopsy incidence, 356
Ureter, amyloidosis, 424
  anastomosis, effect upon conduction of peristaltic waves, electro-ureterographic study, 650
  bone formation, 793
  calculi, 787

  - application of ultrasonic energy to, 865
  - basket bougie for extraction, 55
  - cause of renal colic, 209
- contractility and obstruction in man and dog, 25
- ectopic, opening into seminal vesicle, 57
- electropotential changes, 214
- electroureterography, 650
- epithelial morphology of autogenous grafts when utilized as ureteral and vesical substitutes in dog, 659
- etiology of obstruction and dilatation, 25
- injury during pelvic surgery and radiation on female, 433
- intubation, 43
  - lock splint for, 52
- leukoplakia, 633
- meatotomy, 173
- megalo, 643
- new growths, carcinoma, metastatic from cervix, 242
  - diagnosis, 116
  - prognosis, 119
- obstruction and contractility in man and dog, 25
  - at ureteropelvic junction, 173
  - within bifurcation of kidney artery, 229
- operation for relief of obstruction secondary to compression of upper ureter between dilated pelvis and lower polar artery, 229
- prolapse associated with contralateral meatal stenosis and contracture of bladder neck, 223
- regeneration following experimental segmental resection, 796
  - in repair of experimental ureteral defects, significance of double lumen, 428
  - without intubation, 43
- resection smooth muscle regeneration in repair of experimental ureteral defects, 428
- splint for intubated ureterotomy, 52
  - regeneration without, 43
- stenosis of meatus associated with true prolapse and bladder neck contracture, 223
- substitute, 659
- ureterectomy, 173
- ureterocele, 173
- ureterolithiasis, cause of acute renal colic, 209
- ureterolithotomy, 787
- ureteropelvic obstruction, 1
- ureterosigmoidal anastomosis, 173
- ureterostomy catheters, method of retaining, 1019
  - cutaneous, modified catheter for drainage, 875

Urethra amyloidosis, 122
  - dilatation for passage of resectoscope by new Timberlake obturator attachment 878
  - hypospadias, radical operation for cure of stricture, 501
  - injury, 81
  - intraurethral verruca acuminata in men, 717
  - new growths, carcinoma 514
    - carcinoma complicating prostatic adenocarcinoma, 314
    - carcinoma diagnosis, 505
      - pathology, 505
  - operation for carcinoma, 514
  - stricture, Johanson urethroplasty, 805
    - radical operation 501
  - urethritis bacteria associated with trichomonas vaginalis, 711
  - urethrocystography in differential diagnosis of prostatic cancer, 995
  - urethrography, new diagnostic method for detection of urethral diverticula in female 753
  - urethroplasty for repair of strictures, 805

Urinary tract, amyloidosis 122
  - calculi application of ultrasonic energy to, 865
    - experimental 592 602
    - formation mechanism, 216
  - congenital obstructions in children, 173
  - infections, antimicrobial agents, 892
    - elkosin, gantrisin, triple sulfa, triple sulfa achromycin, 339
  - retrograde infection along indwelling catheter drainage system, 737
  - schistosomiasis, bladder contracture associated with, 671

Urine, bacterial flora of specimens from normal adults, 562
  - detection of blood by simple test, 743
  - diversion of stream by ileal conduit, 470, 950
  - formation, processes involved in, 200
  - hematuria, significance in young men, 135
  - incontinence in Leriche syndrome, 961
  - Papanicolaou technique of staining, 551, 734

  residual, elimination in presence of hypotonic bladder by partial cystectomy, 456
    radiographic estimation in children, 263
  retention in bladder due to drugs, 342
  state of calcium in, 592
  urinalysis, simple test for detection of occult blood, 743
Urogenital tract, amyloidosis, 122
Urography, see also Aortography, Electroureterography, Retroperitoneal Pneumography, Venography, etc.
  cystography in children, 151
  estimation of residual urine in children by, 263
  excretory, allergic manifestations of intravenous urokon, 1011, 1016
    effect of intravenous benadryl in allaying allergic manifestations of intravenous urokon, 1016
    importance of, during episodes of pain for diagnosis of intermittent hydronephrosis, 767
    miokon for, 758
    nephrography during, 572
    reactions due to intravenous urokon, 1011
  kidney, diagnosis of neoplasms, 615
  umbradil, use for urethrography and detection of urethral diverticula in female, 753
  urethra, new diagnostic method for female urethral diverticula, 753
  urethrocystography in differential diagnosis of prostatic cancer, 995.
Urokon, intravenous injections, reactions due to, 1011, 1016
Urology, female, bladder, amyloid tumor, 687
  bladder, atonic, neurogenic, in porphyria, 465
    dermoid cysts, 801
    fistula, vesicovaginal, 75
    incontinence in Leriche syndrome, 961
    injury during pelvic surgery and radiation, 433
    interstitial cystitis treated by transurethral intramural injection of hydrocortone hyaluronidase, 63
    metastatic adenocarcinoma from breast, 965
    tumors, modified position for transurethral resection, 73
    use of Foley catheter for control of stress incontinence, 79
  kidney, suppuration and postpartum candidiasis, 930
  ureter, electromyograms, 244
    injury during pelvic surgery and radiation, 433
    megalo, 643
    metastasis from epidermoid carcinoma of cervix, 242
  urethra, diverticula, new diagnostic method, 753
Urology, pediatric, bladder, cystoscopy, hypothermia induced by, 1006
  cystography, 151
  kidney, simple cysts, 912
  solitary, resection, 900
  spina bifida, complications, 537
  ureter, megalo, 643
  urinary tract obstructions, congenital, 173
  urography, estimation of residual urine by, 263
Urology, war, bladder paralysis, 10-year followup of World War II paraplegics, 66
  urethra, injuries, 81
Uterus, cervix, carcinoma metastatic to ureter, 242

Vagina, fistula, vesicovaginal, 75
Vas deferens, anastomosis, 300
Vein, arteriovenous aneurysm of kidney, 586
Vena cava, contrast filling for diagnosis of renal neoplasms, 615
Vermeulen, C. W., Miller, G. H. and Chapman, W. H. Experimental urolithiasis: X. On state of calcium in urine, 592
Vermeulen, C. W., see M. D. Slominski-Laws, jt. auth.
Vest, S. A., see E. L. Corey, jt. auth.
Vitamin D, effect on citrate excretion, 216

Waisbren, B. A., see D. M. Appleton, jt. auth.
Wald, A. M. Nephrography during routine excretory urography, 572
Wallach, J. B., Glass, Macellis and Angrist, A. A. Autopsy incidence of uremia, its clinical implications, 356
Warren, K. C., see T. R. Fetter, jt. auth.
Watson, J. H. L. Electron microscopy of cystine urolith, 940
Watson, J. S., see J. A. Benjamin, jt. auth.
Webb, E. A. and Smith, B. A. Radical perineal prostatectomy, 1000

Weight change in patients undergoing transurethral prostatic resection, 824
Weinberg, S R, see F C Hamm, jt auth
Weiss, A A, see Michael Kenney, jt auth
Wesolowski, S P, see T H Sweetser, jt auth
Weyrauch, H M and Prest, J C Papanicolaou examination of urine in diagnosis of urinary cancer 2 False positives in diagnosis of renal neoplasms 551
Whitaker, J D, see J B Davis jt auth
Wilk, S P, see J H Woodruff jt auth
Williams, J O, see V H Youngblood jt auth
Williams, M J and Klein, I I Prostatic adenocarcinoma complicated by development of epidermoid carcinoma of urethra, 314
Wolan, C T, see C L Prince jt auth
Woodruff, J H Jr, Chalek, C C Ottoman, R E and Wilk, S P Roentgen diagnosis of renal neoplasms 615
Wormer, D C, Martin, W J, Lauretz, J L and Devine, K D Cutaneous metastasis from carcinoma of bladder, 657

X ray, see Urography
therapy, deep, see Radiation

Yarbro, C L Influence of diet on urinary citrate excretion, 216
Young, B W, Anderson, W L and Ki G G Radiographic estimation of residual urine in children, 263
Youngblood, V H, Williams, J O and Tuggle, Allan Reactions to intra[illegible] urokon, 1011
Yttrium 90, 881
Yttrium chloride therapy for prostatic carcinoma, 837

Ziems, C M, see H M Free, jt auth

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VOLUME 75

BALTIMORE
THE WILLIAMS & WILKINS COMPANY
1956

CONTENTS

JANUARY-JUNE 1956

NUMBER 1 JANUARY 1956

Hydronephrosis *T E Gibson* 1
Pyelectasis *Robert Lich, Jr , J E Maurer and W L Barnes* 12
Pelvic Fused Kidney *A L Miller Jr A W Brown and G C Tomskey* 17
Osteogenic Sarcoma Involving Left Kidney *H C Hudson* 21
Ureteral Obstruction and Contractility in Man and Dog *J A Benjamin, J J Bethell V M Emmel, G H Ramsey and J S Watson* 25
Experimental Studies of Regeneration of Ureter without Intubation *F C Hamm and S R Weinberg* 43
Use of Lock Splint in Intubated Ureterotomy *J R Rinker* 52
A Basket Bougie for Extraction of Ureteral Calculi *H S Browne* 55
Ectopic Ureter Opening into Seminal Vesicle *A E Goldstein and Eugene Heller* 57
Interstitial Cystitis Treatment by Hydrocortone *J L Schulte and L R Reynolds* 63
Status of World War II Paraplegic *A H Lord and R C Bunts* 66
Modified Position for Transurethral Resection of Bladder Tumors in Women *R A Hancock* 73
Vesicovaginal Fistula *B S Azoury P L Scardino and C L Prince* 75
Use of Vaginal Balloon Catheter for Stress Incontinence in Women *C A W Uhle and C C Mackinney* 79
Urethral Injuries *S D Petkovic* 81
Dilution Hyponatremic Shock Another Concept of Transurethral Prostatic Resection Reaction *R H Harrison III, J S Boren and J R Robison* 95
Radical Retropubic Prostatectomy for Carcinoma *Lytle Atherton and L D Atherton* 111
Prostatic Enzymes and Abnormal Bleeding *L A Z Scott* 116
Primary Amyloidosis of Lower Genitourinary Tract *J H McDonald and N J Heckel* 122
Cortisone in Treatment of Epididymitis *T J Florence* 133
Significance of Hematuria in Young Men *Edward Gartman* 135
Use of L Tartrate in Determining Prostatic Serum Acid Phosphatase *Gordon Mathes, S G Richmond and D H Sprunt* 143
Cystography in Children *E C St Martin, J H Campbell and C M Pesquier* 151
Abdominal Venography in Urological Diagnosis *J J Kaufman D E Burke and W E Goodwin* 160
New Technique of Translumbar Aortic Catheterization *Jorge Cuellar* 169

NUMBER 2 FEBRUARY 1956

Congenital Urinary Tract Obstructions in Children *T R Fetter and K C Warren* 173
Mechanisms of Hydronephrosis *Lester Persky F J Bonte and George Austen Jr* 190
Perinephric Abscess Producing a Pneumonephrogram *Robert Braman and R R Cross, Jr* 194
A Low Lying Left Kidney *R E McClellan* 198
Intrinsic Renal Function *J G Edwards* 200
Effect of Temperature, Humidity and Dehydration on Formation of Renal Calculi *C L Prince, P L Scardino and C A Wolan* 209
Influence of Diet on Urinary Citrate Excretion *C L Yarbro* 216
True Prolapse of Ureter *Michael Greenfield* 223
Relief of Upper Ureteral Obstruction Within Bifurcation of Renal Artery *N S R Maluf* 229
Metastatic Carcinoma of Ureter *J J Robbins and Robert Lich, Jr* 242
Electropotential Changes in Normal Human Ureter *E L Corey, E H Fite, Jr and S A Vest* 244
Electrourogram, II Experimental Study *A W Kneucker* 250
Cystitis Emphysematosa *J W Lane and Paul Francke* 256
Management of Hunner's Ulcer by Differential Sacral Neurotomy *M K Moulder and A M Meirowsky* 261
Radiographic Estimation of Residual Urine in Children *B W Young, W L Anderson and G G King* 263
Studies of Urinary Incontinence in Men *F A Beneventi and V F Marshall* 273
Testicular Dysgenesis in Relation to Neoplasm of Testicle *A R Sohval* 285
Use of Scrotal Skin to Cover Wound Defects in Groin and Pubic Area *J S Arconti and W E Goodwin* 292

Intrascrotal Adenomatoid Tumor. *Charlotte Curtiss and Ernest Hock* 297

Anastomosis of Vas Deferens: Experimental Study. *S S Schmidt* 300

Prophylactic Use of Chloramphenicol in Transurethral Prostatic Resections. *D. M. Appleton and B A. Waisbren* 301

Prostatic Adenocarcinoma Complicated by Development of Epidermoid Carcinoma of Urethra *M J. Williams and E. I. Klein* 314

Lipids in Prostate Gland of Dog *A R. Seaman* 324

Sclerosing Lipogranulomas of Male Genitalia. *A R. Marcial-Rojas, J. E. Colon and J. J. Figueroa* 334

Response of Urinary Tract Infections Treated by Elkosin, Gantrisin, Triple Sulfa or Triple Sulfa-Achromycin. *W. E. Clapper and L. E. Plank* 339

Acute Urinary Retention due to Drugs. *S. J. Schneierson and Harry Bergman* 342

Paraplegia, a Rare Complication of Translumbar Aortography. *B. S. Abeshouse and A. T. Tiongson* 348

Autopsy Incidence of Uremia *J. B. Wallach, Macellis Glass and A A Angrist* 356

Clearance Speed: A New Clearance Method. *Hans Clausen* 361

Clearance Without Prolonged Infusion. *Hans Clausen* 364

NUMBER 3, MARCH 1956

Plastic Repair of Hydronephrosis. *J. S. Gardner* 367

Current Status of Chemotherapy of Renal Tuberculosis *J. K. Lattimer and A. L. Spirito* 375

Aneurysm of Renal Artery. *R M Nesbit and W. B. Crenshaw* 380

Pathology of Tumors of Renal Pelvis and Ureter. *J. T MacLean and V. B. Fowler* 384

Diagnosis of Tumors of Renal Pelvis and Ureter. *V J. O'Conor* 416

Prognosis of Primary Tumors of Renal Pelvis and Ureter. *J. E. Dees* 419

Localized Amyloidosis of Ureter. *D. R. Higbee and W. D. Millett* 424

Smooth Muscle Regeneration in Repair of Experimental Ureteral Defects. *Frank Hinman, Jr. and Rudolf Oppenheimer* 428

Diagnosis of Urologic Complications in Gynecology. *Carl Rusche* 433

Treatment of Urologic Complications in Gynecology *Edgar Burns and Irving Peiser* 438

Is Cystitis Cystica an Innocent or a Malefic Lesion? *R. M. Nesbit* 443

Exstrophy of Bladder: Treatment by Plastic Surgery. *T. H. Sweetser, T. C. Chisholm, W. H. Thompson, E. B Berglund, S. P. Wesolowski and T. H. Sweetser, Jr.* 448

Partial Cystectomy for Hypotonic Bladder *C. D. Creevy* 456

Atonic Neurogenic Bladder in Porphyria. *A. G. Redeker* 465

Ileal Loop Diversion: Its Application to Treatment of Neurogenic Bladder Dysfunction. *W. F. Leadbetter and F. G. Shaffer* 470

Study of 2678 Patients with Initial Carcinoma of Bladder. I. Survival Rates. *F. K. Mostofi* 480

Study of 2678 Patients with Initial Carcinoma of Bladder II. Survival Rates in Relation to Therapy. *F. K Mostofi* 492

Radical Operation for Cure of Intractable Stricture of Male Urethra. *A. B. Cecil* 501

Carcinoma of Male and Female Urethra: Pathology and Diagnosis. *A. L. Dean* 505

Treatment of Urethral Tumors. *R H. Flocks* 514

Effect of Cortisone on Spermatogenic Function of Human Testes. *J. H. McDonald and N J Heckel* 527

Dependent Drainage Via Perineum in Retropubic Prostatectomy. *Richard Chute and E F Ireland, Jr* 530

Urological Complications of Spina Bifida in Children. *P. A. Morales, G. G. Deaver and R S Hotchkiss* 537

Papanicolaou Examination of Urine in Diagnosis of Urinary Cancer. *H. M. Weyrauch* and *J C Presti* 551

Effect of ACTH Administration on Urinary Excretion of Androgens and Other Steroids by Old Men in Comparison with Young Men. *D. A. MacFarlane, C. B. Leman, P L Munson and J. H. Harrison* 558

Bacterial Flora of Urine Specimens from Normal Adults. *V. B. Philpot, Jr.* 562

Air Embolism During Presacral Pneumography. *Irving Glassman, Robert Shapiro and Franklin Robinson* 569

Nephrography During Routine Excretory Urography. *A. M. Wald* 572

NUMBER 4, APRIL 1956

Nonhormonal Adrenal Adenoma. *Wilfred Gordon* 579

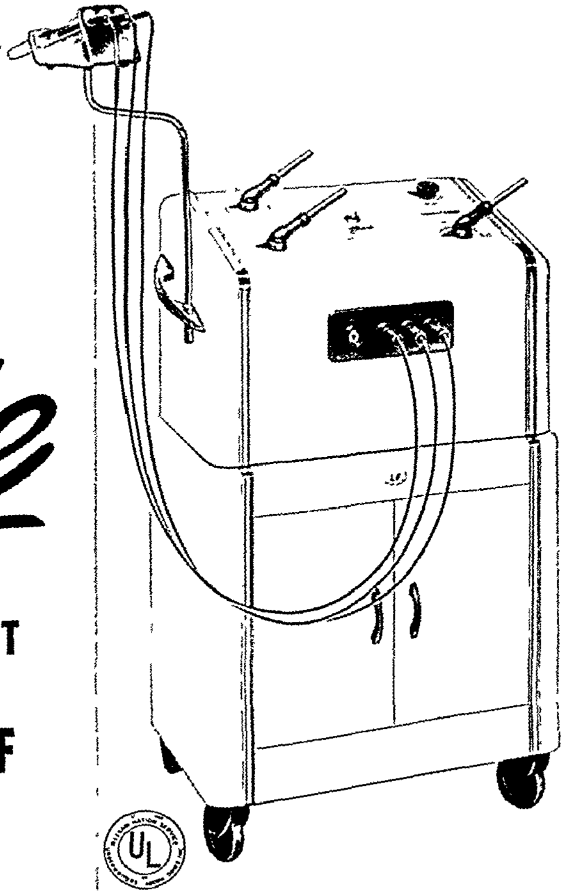
Arteriovenous Aneurysm of Kidney. *M. D. Slominski-Laws, J. H. Kiefer and C. W. Vermeulen* .. 586

Experimental Urolithiasis: X. On State of Calcium in Urine. *C. W. Vermeulen, G. H. Miller and W H. Chapman* . 592

Urolithiasis in Mink: Pathology, Bacteriology and Experimental Production. *Iver Moller Nielsen* .. 602
Roentgen Diagnosis of Renal Neoplasms. *J. H. Woodruff, Jr., C. C. Chalek, R. E. Ottoman and S. P. Wilk* 615
Tubular Carcinoma of Kidney Within a Solitary Cyst. *Heino Provet, J. R. Lisa and Salvatore Trinidad* 627
Leukoplakia of Renal Pelvis and Ureter. *V. A. Politano* . 633
Megaloureter. *E. L. Lewis and R. W. Cletsoway* 643
Effect of Ureteral Anastomosis Upon Conduction of Peristaltic Waves: An Electro- *her, Jr. and William Sleator, Jr.* 650
Epit Grafts When Utilized as Ureteral and Vesical al. *A. R. Sanders and C. J. Schein* 659
Comparative Study of Effect of Anticholinergic Drugs on Human Bladder Stimulated by Furmethide. *J. W. Draper and Mieczyslaw Sierp* 665
Fibrotic, Contracted Bladder Associated with Schistosomiasis and Chronic Ulceration. *E. S. Sayegh and R. M. Dimmette* 671
Classification of Carcinoma of Bladder Associated with Schistosomiasis and Metaplasia. *R. M. Dimmette, H. F. Sproat and E. S. Sayegh* 680
Amyloid Tumor of Bladder. *P. H. Hartz and Ernesto Santander* 687
Clinical Implications of Transplantability of Induced Bladder Tumors to Intact Tran- in Dogs. *D. F. McDonald and Theodore Thorson* 690
Surgical Implantation *Frank Hinman, Jr* 695
oma of Bladder *D. C. Wormer, W. J. Martin, J. L. Emmett and* 697
Carcinoma of Bladder with Cutaneous Metastasis *A. J. Bischoff and B. G. Fishkin* 701
Bacteria Associated with Trichomonas Vaginalis in Male Urethritis *L. G. Feo, T. R. Fetter, D. M. Peoples and H. E. Morton* 711
Intraurethral Verruca Acuminata in Men. *Edward Gartman* 717
Fournier's Gangrene of Penis and Scrotum *J. F. Thomas* 719
Carcinoma of Penis due to Trauma Occurring in a Male Patient Circumcised at Birth *R. D. Amelar* 728
Eosinophilic Granulomatous Prostatitis *W. M. Nickey and P. O'B. Montgomery* 730
Exfoliative Cytology as Screening Method in Prostatic Carcinoma. *J. M. Silberblatt, Cyril Solomon and R. M. Hyman* 734
Retrograde Urinary Infection Along Indwelling Catheter Drainage System in Paraplegia *Michael Kenney, A. A. Weiss, H. C. Lindenauer, E. F. Delagi, G. B. D'Oranzio and A. S. Abramson* 737
Studies with Simple Test for Detection of Occult Blood in Urine *H. M. Free, A. H. Free and A. S. Giordano* 743
Positive Pressure Urethrography: A New Diagnostic Method. *H. J. Davis and L. G. Cian* 753
Miokon, A New Intravenous Urographic Medium. *C. H. Nicolai* 758
Program, Annual Meeting, American Urological Association 761

NUMBER 5, MAY 1956

Diagnosis of Intermittent 767
Solitary Serous Cysts of K *and Eli Dubinsky* 772
Cystic Disease of Renal Py *Collins* 776
Renal Vein Thrombosis. *W. C. Eikner and C. J. Bobeck* 780
Acquired Renocolic Fistula in Remaining Functioning Kidney with Recovery. *G. S. Rost, Dean Cooper, Knouf, Paul Ferguson and Ashton McCrary* 787
Bone Formation in Ur 793
Ureteral Regeneration *W. L. Huffman, H. F. McCorkle and Lester Persky* 796
Dermoid Cysts of Bladder. *E. W. Caulfield* 801
Johanson Urethroplasty for Repair of Urethral Strictures *D. J. Jaffar, G. R. Sewell and F. W. Schwarz* 805
Incarcerated Scrotal Appendicitis *J. R. Herman* 811
Duplication of Left Undescended Testicle *Saul Kay and F. P. Coleman* 815
Bilateral Adenomatoid Tumor of Epididymis *L. J. Morin* . 819
Absorption of Irrigating Solution and Associated Changes upon Transurethral Prostatic Resection *N. S. R. Maluf, J. S. Boren and G. E. Brandes* 824
Treatment of Carcinoma of Prostate with Radioactive Materials. *G. J. Bulkley, J. A. D. Cooper and V. J. O'Conor* .. 837
Complications Associated with Urological Diagnostic Methods. *William Baurys* . 846
Treatment of Male Infertility with Estrogenic Substance. *W. M. Kearns* . . 852
Phosphatase Activities of Various Human Tissues. *Hans Marberger, R. D. Riedesel, D. O. Anderson and L. H. Malek* 857



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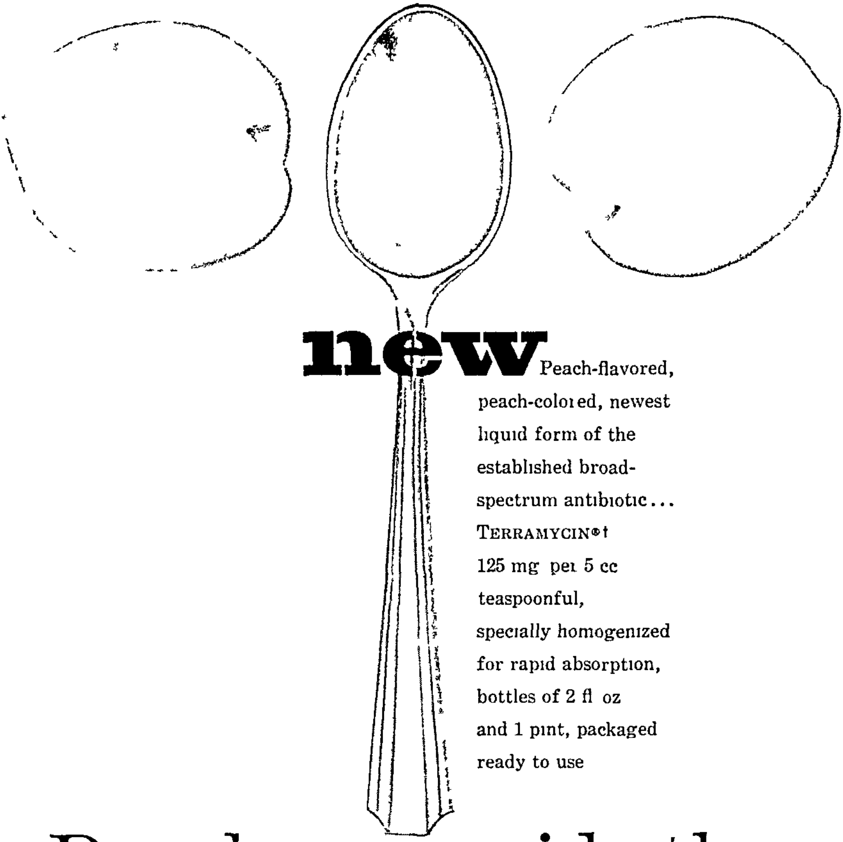

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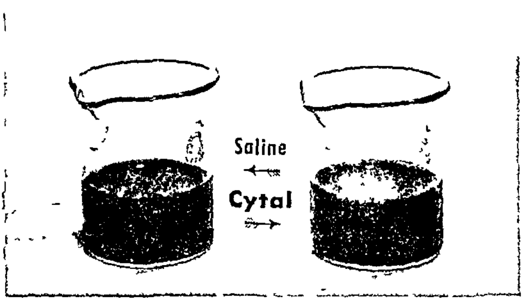

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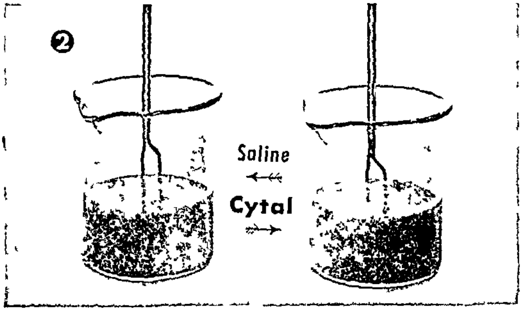

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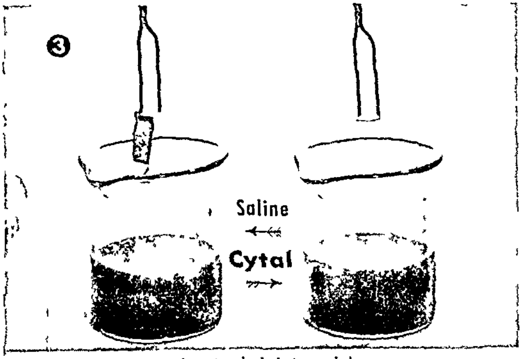

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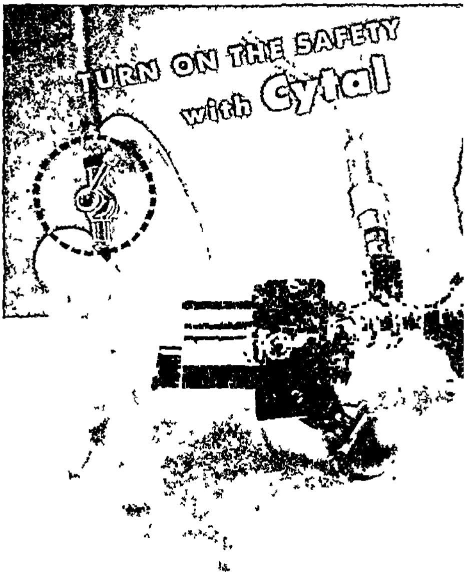

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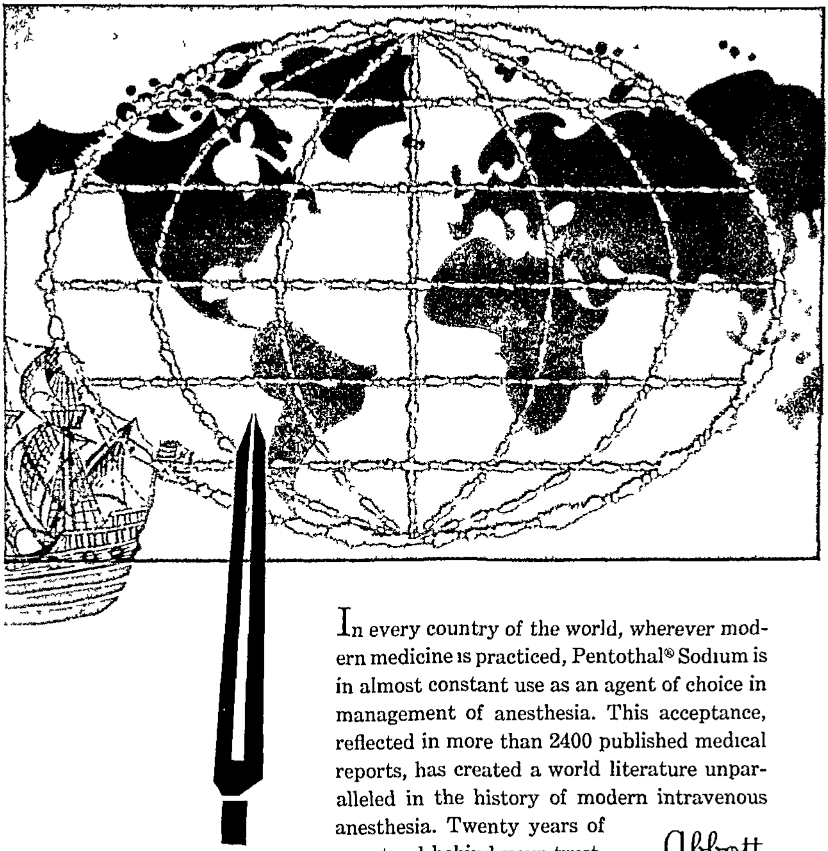

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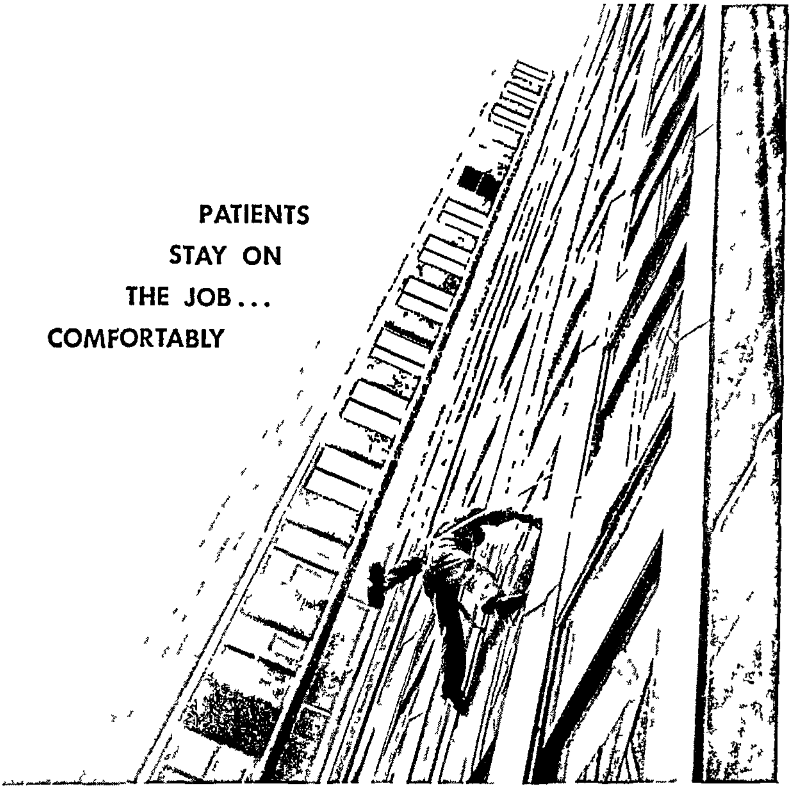

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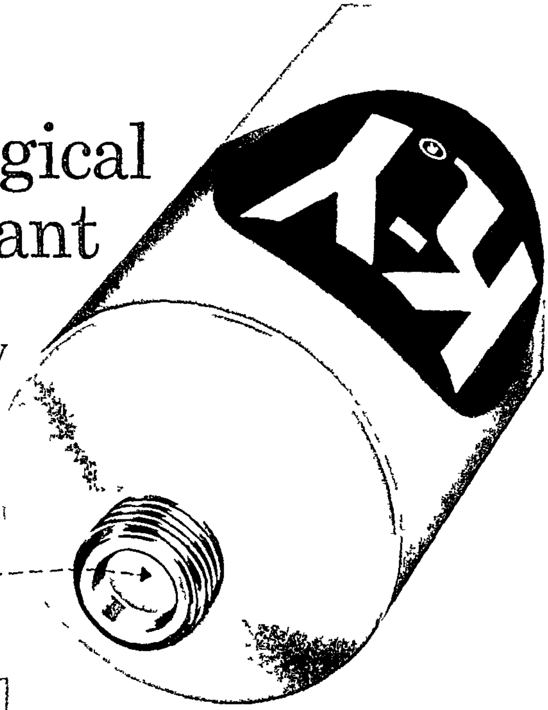

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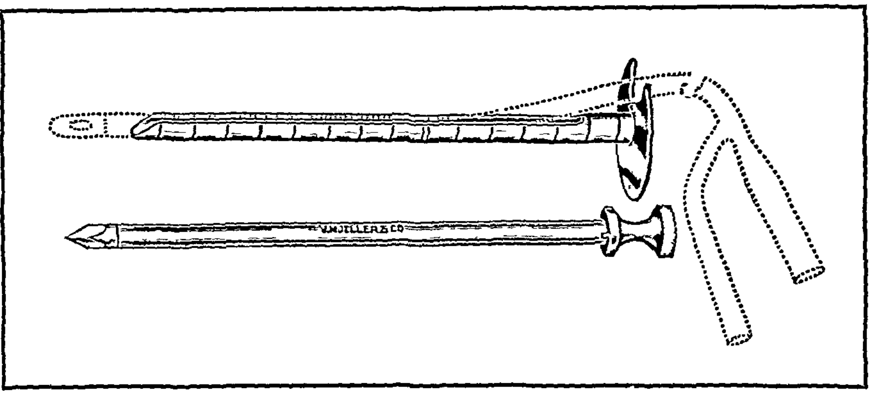

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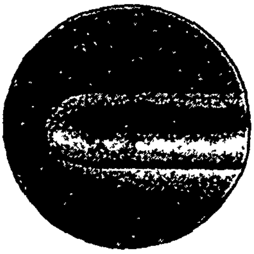

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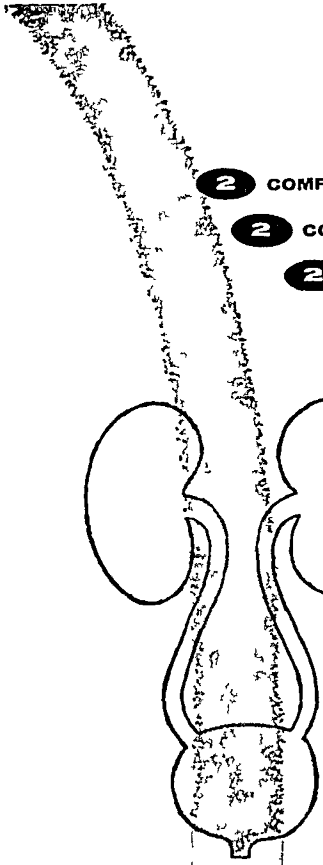

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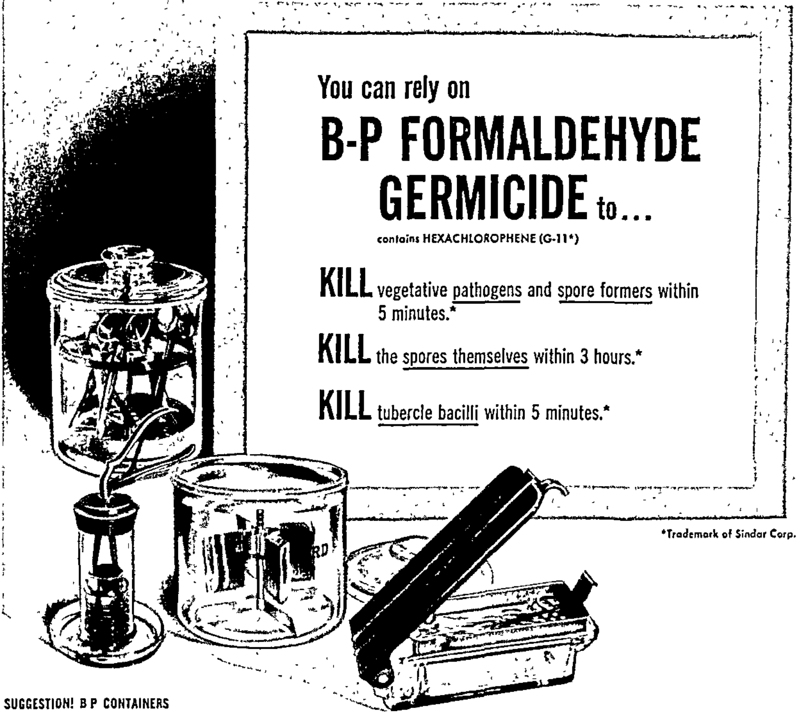

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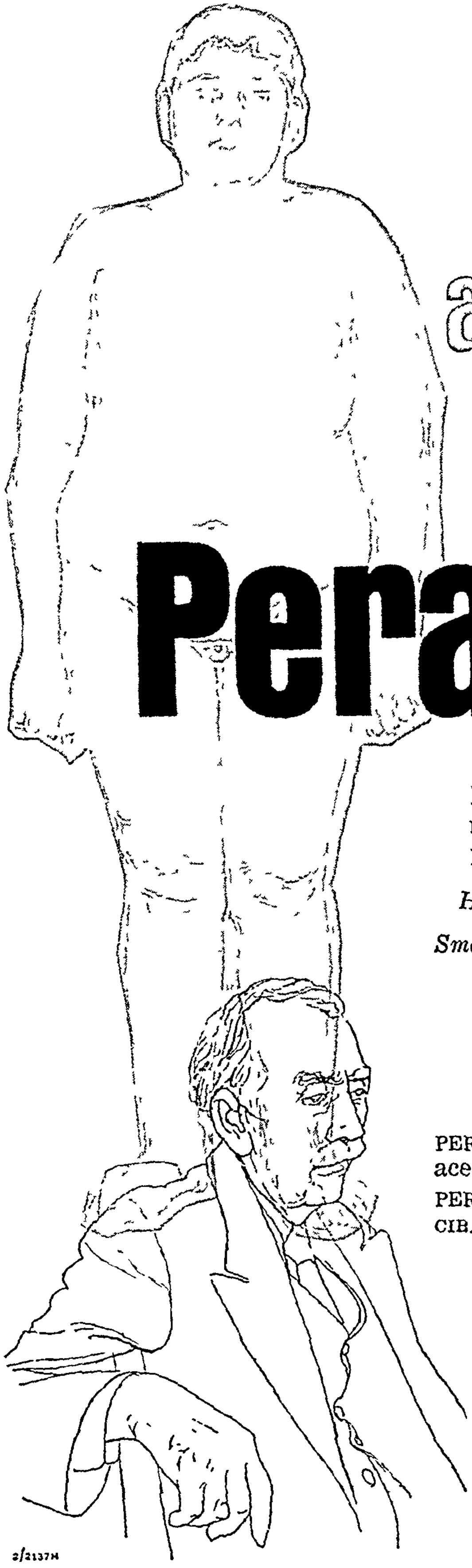

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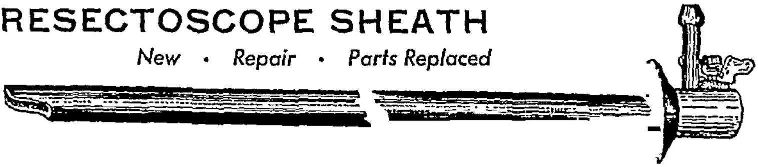

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